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MICROSCOPICAL MORPHOLOGY.

MICROSCOPICAL MORPHOLOGY

OF THE

ANIMAL BODY

IN HEALTH AND DISEASE.

BY

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WITH 380 ORIGINAL ENGRAVINGS.

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PREFACE.

IN presenting this book, the result of ten years' intense labor, to the public, I am aware that not all the facts and conclusions here laid down will meet the immediate approval of professional microscopists.

The cell-theory, which for more than thirty years held sway over the minds of scientists, was contradicted by me in 1873, when I demonstrated the continuity of all elements engaged in the construction of tissues. In 1872, I discovered the connections between cartilage-corpuscles, which, thanks to a simplified method, are now easily seen. Shortly afterward, the intimate structure of "protoplasm" was discovered, and it was found that the same structure is present throughout all the interstitial substances which had hitherto been considered lifeless.

As many of the assertions made in 1872 and 1873 have already been found correct by good observers, I confidently expect that the others too will, in time, be accepted, although directly contrary to the cell-theory.

In the autumn of 1874 I left Vienna, and, on the first of November of the same year, opened a laboratory for microscopical investigation in New-York. This has proved successful beyond all expectation. Over seven hundred attendants, among them some of the most intellectual and independent members of the medical profession, have here satisfied themselves of the correctness of my assertions. A number of these have made valuable investigations in my laboratory, the results of which will be found embodied in various articles in this book.

In view of these facts, I can await patiently the approval of scientists abroad. A doctrine which is accepted by good observers in America cannot be lost, but will develop independently of European microscopists, who, to a great extent, are prejudiced by the teachings of the older masters.

Again have facts made it evident that the United States of America are ahead whenever new ideas of practical importance are to be acknowledged. I have received, in New-York, much encouragement from my students and co-workers. I have also been magnanimously supported by a friend, who is not a medical man, but a prince in character and wealth, and who surpasses most European princes in that he will not allow me to inscribe his name upon the dedicatory page.

The illustrations of this book are, without exception, my own drawings, and have been transferred on metal to my complete satisfaction by the Moss Engraving Company, of this city.

C. HEITZMANN.

39 WEST 45TH STREET, NEW-YORK, August, 1882.

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I.

METHODS.

THE methods of preparation of the liquid and solid constituents of the animal body are of the utmost importance. Every progress in histology is largely due to an improvement in the methods of preparation employed as well as of the optical apparatus.

The main purpose obviously must be to examine liquids and tissues in a condition as nearly as possible like that in which they exist within the living body. The history of histology teaches that the greatest errors have resulted from a neglect of this rule. From the moment a specimen for examination with the microscope is allowed to dry, such a specimen has become a mummy, and unfit for further research. Almost all tissues, in former times, were allowed to dry before their minute structure was examined. The results of such researches are considered worthless nowadays. Despite of all experience gained in the last four decades,—that is, the time in which microscopic morphology has gradually developed into a science,—even in our day, dry bone-tissue is examined in all laboratories; but such examinations are necessarily of very small value. Another objectionable procedure is the tearing, teasing, and pulling of tissues. By such methods, the parts which in the body are connected become broken and disfigured, *débris* are produced, sometimes with the greatest skill, which, as a matter of fact, are useless for fruitful microscopic investigations. Both mechanical and chemical isolation of the constituent parts of tissues should be used to a very limited degree only. Just as objection-

able is boiling, or a complicated chemical treatment, which, as a rule, yields results far from the truth.

Infusion. Among the liquids useful to be examined for biological purposes first ranks the "infusion." Torn blades of grass are, with the careful avoidance of the admixture of particles of earth, transferred to a china soup-plate, common water is poured upon them, and they are left uncovered and undisturbed at the temperature of the laboratory. To make up for evaporation, some water may cautiously be added from time to time. After from six to ten days, sooner in summer than in winter, this liquid will swarm with newly formed organisms, the study of which is most fascinating to the biologist. A droplet of the infusion is brought on a glass slide, covered with a thin covering-glass, and is a ready specimen for microscopic research.

If we mix together some water with organized bodies, such as grass, apparently destined to decay, there will sprout up a remarkably rich generation both of plants and animals. To explain this fact is quite difficult. Some observers believe that the decaying particles of vegetables themselves change into new organisms under favorable circumstances; while others, and doubtless the majority, are of the opinion that there are floating in the air millions of invisible germs of plants and animals, which, on finding a favorable soil for development, begin to grow and prosper. The germ-theory, first thoroughly established by Pasteur, has not as yet been contradicted in a satisfactory manner; we have, therefore, every reason still to adhere to it. Certainly no development of infusoria takes place if the air be prevented from reaching the infusion.

Among the numerous organisms in a drop of infusion perhaps the most elementary is the amœba, which is best obtained from the border of the infusion in the plate, or from the blades of the decaying grass, gently scraped with a knife. The amœbæ are pale, with lower powers of the microscope finely granular, transparent lumps, which continually change their shape and locality. In the first few weeks after the preparation of the infusion, we obtain amœbæ of the shape and motion of caterpillars, which are the most suitable for microscopic examination, especially if in slow motion.

It is remarkable that I succeeded in raising almost identical forms of living organisms on mixing together the same material several thousand miles away from New York, viz., in Vienna. There is a slight difference, however, important enough to be mentioned. In Vienna I never saw an amœba without a distinct lump in its interior, the nucleus; while in New York, the more common occurrences are amœbæ without nuclei. As these animalcules are identical in every other respect, both in Vienna and New York, this fact

disproves the opinion of many histologists that the nucleus is something essential to the so-called "unicellular" organism. Haeckel's view, viz., that there is a marked difference between forms devoid of a nucleus, termed by him "cytodes," and those with nuclei, termed "cells," must be considered to be untenable.

Moist Chamber. Von Recklinghausen invented the moist chamber for the purpose of preventing microscopic specimens from evaporation, without cutting off the supply of air. Many devices have been invented for this purpose. One of the simplest is L. Ranvier's—a slide on which a circular furrow, for holding air, surrounds the central plane surface; on the latter a droplet of the liquid is placed, and the covering-glass, which must be large enough to cover the whole of the furrow at its edges, is hermetically sealed to the slide by a frame of melted paraffine. S. Stricker uses a slightly elevated frame of glazier's cement, on the top of which he sticks the covering-glass holding the specimen, while a droplet of water on the bottom of the chamber supplies moisture. The same investigator uses a moist chamber, which, for examinations not exceeding one or two hours' duration, proves to be the best and simplest of all. He oils the edge of one side of the covering-glass, and after having transferred a droplet of the fresh liquid to the slide, he covers it so that the oil-frame of the covering-glass adheres to the surface of the slide around the specimen.

Heatable Stage. Max Schultze introduced the so-called heatable stage with the view of keeping up in a specimen the temperature of the body, or raising it at will. As a matter of course, liquids of cold-blooded animals, especially their blood, need no such apparatus. A droplet of blood of the newt (triton, salamandra), which we obtain by cutting off the end of the tail of the animal with a pair of scissors, may be transferred upon the slide by simply touching the wound. The specimen must immediately be covered with a very thin covering-glass, the edges of which have been oiled beforehand. With a little skill, a specimen is obtained fit for examination even with the highest powers of the microscope. The warmer the temperature of the room the sooner the colorless blood-corpuscles will begin to change their shape and location. They will prove to be identical with the amœbæ found in an infusion of grass. The examination of the colorless blood-corpuscles, or other isolated bioplasson bodies of warm-blooded animals, by means of the heatable stage, has proved their identity also with amœbæ. Such bodies within the

tissues may, as long as they remain alive, exhibit under the heatable stage changes of shape, but, on account of their being imbedded in basis or cement substance, no locomotion.

The heatable stage of S. Stricker is a shallow metal case, the central cavity of which is connected with small pipes for the conduction of gases to be brought in contact with the living specimen. The latter rests on the lower surface of the covering-glass. In front of the case a metal peg can be connected with a spiral copper wire, the distal extremity of which is heated over an alcohol or gas lamp. The temperature is shown by a small thermometer outside the case. If a drop of blood be inclosed between two thin covering-glasses, with greased edges, the phenomena of amœboid motion and locomotion are much better observed than in a drop hanging on the lower surface of one cover only. For high powers of the microscope, a condenser of light must be put into the diaphragm of the stage, as a good deal of light is lost on account of the unavoidable depth of the stage.

Electricity. Living specimens are sometimes exposed to the influence of the electric current, preferably the induced, interrupted, as that alone admits of proper action upon the specimen. Both the constant and an induced current extending over several minutes are objectionable, as electrolysis with formation of gas-bubbles occurs, and the thermic action may destroy the effects of electricity upon the specimen. The simplest apparatus for applying electricity under the microscope is that of E. Brücke. A glass slide is covered with strips of tin-foil, between which, in the center of the slide, rests the specimen. The lower surface of the glass slide, also covered with tin-foil, is moved on two parallel copper supports attached to a larger glass plate, and in connection with the electrodes.

Preparation of Fresh Tissues. Tissues from the freshly killed animal are, as a rule, unfit for microscopic research beyond a limited time. There is no liquid which keeps the specimen unchanged, and, without the addition of some liquid, the specimen soon dries. As preserving fluids have been used the liquid of the anterior chamber of the eye, serum of blood, the amniotic liquid of calf or sheep embryos, with the addition of a little metallic iodine, normal urine, one-half per cent. solution of chloride of sodium, very dilute solution of bichromate of potassa, etc. The two latter answer all purposes. Water is objectionable, as the bioplasson matter swells and becomes destroyed by it; the same destructive action is noticeable on the addition of glycerine.

Fresh specimens, if in the shape of delicate membranes, are spread over the glass slide, while, if in the shape of masses not transparent, they are cut with the razor in a frozen condition. The freezing mixture may be snow or broken ice with salt in one compartment of a metal box, while the other compartment holds the specimen, fixed, if necessary, by mucilage of gum arabic. Numerous freezing microtomes have been invented; in some, rhigolene or ether-spray is produced, by means of which a fresh specimen may in a few minutes be frozen to such a consistence that it can be cut with a razor. Specimens so obtained are useful for temporary examinations or for staining, especially with chloride of gold. Freshly cut specimens may be preserved by the addition of a very dilute solution of bichromate of potassa, which is allowed to flow under the covering-glass, and is drained off by strips of filtering paper held against the edge of the cover.

Preservation of Tissues. The best method of preservation and hardening of normal and morbid specimens is to divide a large mass of the tissue by incisions into small pieces, of one or two inches diameter, and to place these pieces in a wine-yellow solution (one-half per cent.) of chromic acid. The chromic acid is kept ready in strong solution, of which a small quantity is added to the water holding the specimen in a glass jar. It is important that the specimens be placed in a large quantity of liquid, its bulk exceeding that of the specimen at least five or six times. These precautions are necessary, as the hardening action of chromic acid does not penetrate very deeply. In one or two days, the liquid having become cloudy, the chromic acid solution must be renewed, and such renewal is to be repeated every few days until the solution remains clear. Specimens of bone or teeth are treated in the same manner, and the extraction of the lime-salts may be hastened by a very cautious addition of dilute muriatic acid every fourth or fifth day. If the chromic acid be applied in this way, it hardens the tissues in a few days or weeks, with no other change than a slight shrinkage, and renders them fit for cutting with the razor. After the specimens have been hardened, we still may keep them in very dilute solutions of chromic acid, to which we add small quantities of alcohol in order to prevent the growth of mildew, the most unpleasant enemy of a laboratory for microscopic research.

A dark wine-yellow solution of bichromate of potassa is also suitable for the preservation of specimens, though in such a

solution hardening goes on very slowly, or not at all. The hardening may be accomplished by the solution of chromic acid as described above, or by alcohol. The latter method is the best for preservation of brain specimens, which, by the slightest excess of chromic acid, become too brittle to be cut. Eyes are placed fresh into Müller's liquid (two parts of bichromate of potassa, one part of sulphate of soda, and 100 parts of water). After a few weeks the eye may be cut open and transferred into a one-half per cent. solution of chromic acid, or into strong alcohol, in order to accomplish the hardening process. The advantage of these re-agents is that they do not interfere with the structure of the tissue, and render all constituent parts very distinct. Chromate of ammonia or picric acid solutions are by no means superior to the above-described liquids. Alcohol, for preservation of specimens, is objectionable, as it makes the tissues shrink, and leaves them too pale and indistinct for good observation. Specimens kept in alcohol for a while should be placed in a one-half per cent. solution of chromic acid, in which they harden very quickly, and become well adapted for microscopic purposes. Bone and teeth, after a long-continued action of chromic acid, on account of the reduction of the latter, assume a dark green color, without change of their structure.

Cutting. After the specimens have become sufficiently hard, they are ready to be sliced into thin and transparent sections. For this purpose a good razor, flattened on the side which slides on the specimen, is the simplest and most convenient tool. The specimen is rid from chromic acid by being placed in water; it is held in the left hand, flattened out by one stroke of the razor, and the flat surface is kept in a horizontal position over a china soup-plate filled with water. We take up a little water on the hollow surface of the razor, and, while the water runs over the level of the specimen, the razor is drawn slowly and uniformly through the tissue without producing ridges. The thinner the specimen the better. With the assistance of a flat copper spoon and a needle, the thin sections are transferred to a china saucer holding water, in which, if desired, staining re-agents are applied. Common water answers all purposes, and neither alcohol nor distilled water are required. Small or hollow specimens, which cannot be held in the left hand, such as halved eyes, teeth, etc., must be imbedded in the following way: The hardened specimen is placed in strong alcohol for twelve to twenty-four hours, in order to be rid of its water. A square paper box, according to

the size and shape of the specimen, is made; we fill the bottom with a melted mixture of paraffine and wax, six or eight parts of the former to one of the latter, with the addition, perhaps, of a little mutton-tallow. As soon as the layer of the mixture in the box becomes cloudy, the specimen, from which the surplus of alcohol meanwhile was allowed to evaporate, is transferred into the box, and the paraffine mixture, not too hot, is poured over it. The box, when full, is placed in cold water, where the surrounding paper is destroyed, and the fat becomes hard in a short time. The sections are made simultaneously through the paraffine and the specimen, in the same way as described before. No clearing re-agents, such as turpentine or oil of cloves, should be used before imbedding the specimen, as such re-agents render the details of the structure indistinct. Small specimens may be fitted into two pieces of the best so-called velvet-cork, properly hollowed out, and cut together with the cork.

Everybody can learn to cut sections by more or less practice, though a certain amount of cleverness and steadiness of the hands is required to reach perfection. The rule is, that the section should be very thin, transparent, while its size is of much less importance. Valuable specimens, of which very little ought to be lost, may be cut with a section-cutter. The simplest style is a metal tube mounted at right angles with a circular black-glass or India-rubber plate. The central perforation of the plate opens into a cylindrical metal box of varying diameter, which, by means of a screw, slides within the metal tube. The paraffine mixture is poured into the metal box, and the imbedded specimen is gradually lifted to the level of the plate, over which the flat surface of the razor-blade is passed. Complicated cutting-machines, in which the blade of the knife works on the principle of a plane, are invented in large number, and prove to be satisfactory in the hands of their inventors, or whenever a large number of specimens is required for distribution or for trade. The greater the complication, the less is the value of such machines.

Mounting. The sections, after being stained, are transferred on a metal spoon with the assistance of a needle. The best spoon for the purpose is one made of hammered copper wire, the flattened and rounded extremity of which is at a right angle to the wire, the latter constituting the handle. Perforations of the spoon are superfluous. The surplus water is soaked away from the lower surface of the spoon by means of good white

filtering-paper; a drop of dilute glycerine is added—best with the glass stem of the bottle holding glycerine—to the specimen, which is then worked down to the center of a glass slide. Here the specimen is spread out, if necessary, with two needles, its position corrected, and the covering-glass gently placed over the drop, so as to avoid including air-bubbles. With a little practice and skill we learn to add the exact quantity of glycerine. Should the drop prove to be too small,—viz., if a corner or edge of the covering-glass wants glycerine,—a small droplet is approached to that edge, and will flow under by capillary attraction. If too much glycerine be taken, it must be drained off by moist filtering-paper, and the slide cleansed carefully with a piece of such paper folded up and moistened. The sealing together of both glasses should be accomplished by painting varnish in the shape of a narrow but heavy rim along the edge of the covering-glass; but great care must be taken to have both slide and cover first absolutely clean and dry.

The only liquid which can be fully recommended for mounting hardened specimens is glycerine in the purest chemical condition, to which distilled water (about one part of water to three parts of glycerine) is added. Mounting in Canada balsam or in damar varnish is objectionable, as the specimens in these liquids in time clear up to such an extent as to become unfit for amplifications of the microscope exceeding 300 or 500 diameters. Long-continued trials, as regards the value of both methods, have led me to this conviction. Specimens of any description, mounted in Canada balsam or in damar varnish, are not suitable as test objects. To-day, the power of definition of a lens should be tested exclusively on living objects, such as infusion organisms, fresh blood corpuscles, saliva corpuscles, etc. The process of mounting in glycerine is simpler and easier than any other method, and, if all precautions mentioned are carried out with care, no change of the specimen will take place. True, glycerine specimens need more careful handling than balsam specimens, but their value is decidedly greater than that of the latter.

In order to make glycerine mounting safe, it is preferable to delay applying the varnish for twenty-four hours, as the surplus water by that time will have evaporated. Should too little glycerine be used, the inclosing varnish will run under the cover and deprive the specimen of its neat appearance; should too much glycerine be left between the two glasses, it often happens that after months or years the glycerine finds its way through

the rim of varnish, and the specimen becomes spoiled. As an inclosing varnish, asphalt dissolved in turpentine is generally used, though any other varnish answers the purpose if put on in sufficient quantity. The mounting and varnishing of glycerine specimens is easier with square than with circular covering-glasses.

Staining. The ammoniacal carmine solution (Gerlach) is the most satisfactory for staining specimens obtained after hardening in chromic acid solution. To the best cochineal powder we add distilled water and a few drops of aqua ammoniæ fortis, until the cochineal is completely dissolved. The amount of the carmine solution to be poured into the saucer holding the sections depends on the concentration of the solution. The best way is to take but little carmine, and let it act on the specimen for twenty-four hours. The various compounds of carmine in use may be dispensed with, as all carmine staining is very unreliable, and, except for the handsome appearance it gives to the specimen, of no material value.

Hæmatoxylon (logwood) and eosine are re-agents used for alcohol specimens exclusively, but not suitable for chromic acid preparations. The action of the picric acid is kindred to that of chromic acid. Aniline colors as a rule are not fast, neither are solutions of picro-indigo.

Osmic acid (M. Schultze) in a one per cent. solution stains fat black in both the fresh and the preserved condition of the specimen; it renders the contours of the tissue, especially nervous tissue, more distinct, but otherwise has a very limited value.

Important re-agents are the nitrate of silver (Von Recklinghausen) and the chloride of gold (Cohnheim); though specimens treated with either of these re-agents become indistinct after five or six years. Nitrate of silver is brought into contact, in a one per cent. or two per cent. solution (kept in black bottles), exclusively with fresh specimens, for only a few minutes, or used for injections into blood and lymph vessels. Distilled water is needed for washing off the re-agent. The solid nitrate of silver may be applied directly on dense tissues, such as cornea or cartilage, though the layers which come in direct contact with the stick are destroyed. Silver-stained specimens are suitable for glycerine mounting.

Chloride of gold is invariably used in a one-half per cent. solution, and is fit for fresh and frozen specimens, as well as for those preserved in chromic acid; in the latter case, after careful

soaking in distilled water. The exposure to this re-agent may vary from fifteen to sixty minutes, or even over this time. After the re-agent is washed off with distilled water, especially for staining nerves, a few drops of acetic, tartaric, or formic acid may be added. Such specimens are mounted in glycerine.

Absolute alcohol (Spina) is a re-agent which has recently become of importance for bringing to view certain features in the varieties of connective tissue. The tissue is kept for only two or three days in alcohol, cut and examined in alcohol, but cannot be preserved.

Injections. In order to render the vessels of a tissue plainly visible, stained liquids are driven into them. The best liquid is fine melted gelatine, stained red with carmine, or blue with soluble Prussian blue. As a rule, the injection is made into a larger artery, whence the liquid spreads through capillaries and veins. The artery is fastened to a small metal or glass tube fitting at one end the caliber of the artery, at the other end the caliber of the tube of the syringe or other apparatus. All other vessels must be ligated except one vein, which, by emptying the injected liquid, indicates a complete filling of the vascular system. Both the gelatine and the tissue must be kept at a temperature preventing coagulation. The injection is made by a syringe, or by more complicated pressure apparatus, which latter, by their slow action, yield better results than the former. Injected specimens are placed and kept in alcohol, as the chromic acid solution destroys the colors added to the gelatine. Spontaneous injection has been used on frogs. So-called parenchymatous injections, in which colored liquids are driven with a pointed syringe directly into the tissue, were thought to be of great value at one time, but they are abandoned nowadays.

How to Work with the Microscope. After a specimen is transferred to the table of the stage of the microscope, and by the coarse adjustment or by pushing the tube is brought into focus, one hand is placed on the fine adjustment, the micrometer screw, and should not be removed during the examination. Both eyes must be kept open, and no ocular accommodative power exercised, as the careful handling of the micrometer screw renders accommodation superfluous. Every specimen should be examined at first with low powers of the microscope, and a gradual increase of the power is accomplished by changing the systems of the objectives. For illumination of the object we use dispersed daylight or kerosene-light, which latter is far superior to gas-light.

For low powers, the plane mirror and the large diaphragm are in order, while higher powers require the use of the concave mirror and small diaphragms. All powers of the microscope exceeding 800 diameters are reached to-day by immersion lenses. If an immersion lens be employed, the microscope should be placed at a certain distance from the window, or else kerosene-light be resorted to. For researches with immersion lenses in daylight, the time between eleven and two o'clock is the best, though light-condensing lenses placed below the level of the specimen may prove useful at other times of the day.

As soon as investigation commences, the note-book and the pencil must be on hand, in order to fix every observation on paper, though even in no better shape than that of a rough sketch. Nobody can be a good observer with the microscope unless he is a draughtsman. If the eyes be not educated in seeing, and the hand in reproducing on paper what the eyes perceive, all efforts to gain correct ideas of what the microscope teaches are in vain. To see with the microscope is a difficult art, requiring many years of thorough education. The assistance of a reliable teacher cannot be dispensed with, for in the art of microscopy no autodidact can reach perfection any more than in any other art. Learn to draw, if you desire to see with the microscope.

A number of devices have been invented for facilitating the drawing of microscopic specimens by means of prismatic glasses. All these are superfluous. If we want to represent a microscopic image on paper, exact in size and shape, we place the paper at the height of the stage of the microscope, very near the right side of the specimen. Looking into the eye-piece with the left eye, keeping the right open, the image is seen projected on the paper, and the point of the pencil can exactly follow the outlines on the image itself.

A great deal of time is wasted by applying manifold staining methods to microscopic specimens, and they are deceived persons who imagine that the value of a specimen is the greater the nearer it approaches a rainbow appearance. In wasting time by projecting images on screens by means of complicated mechanisms, many forget that microscopy can really be learned only by handling the microscope, and both eyes and judgment can be educated only by looking into the microscope itself. Too great stress is laid, also, on photographing microscopic specimens. Those who are delighted with nice staining of microscopic specimens, splendid projections on screens, and large micro-

photographs, generally lose sight of the aim of the microscope. We have better things to do than to play with methods of staining and projections. We study the relations of physiological and morbid appearances to their anatomical bases—a more serious and difficult task. Photographing microscopical specimens has reached its highest perfection in America, where technical talent is so remarkably developed. Although such photographs are useful in certain respects, their value should not be overestimated, because they are indistinct wherever the specimen is not even, or shows several strata. Under such circumstances, photographs can hardly replace drawings made by an experienced and conscientious observer.

II.

GENERAL PROPERTIES OF LIVING MATTER.*

LIVING, or organized, matter is the substance which builds up plants as well as animals—the simplest infusorium as well as the most highly developed mammal.

Chemistry. The question what living matter really is, cannot yet be answered from a chemical stand-point, and there is reason to doubt whether it ever will be settled, inasmuch as it is impossible to obtain pure living matter in a quantity sufficient for chemical analysis. As every substance, also, the living matter must necessarily be composed of minute particles, which can never be seen, even with the highest magnifying powers, *i. e.*, the simplest units, the so-called molecules, which admit of no further division. After Elsberg's at present almost generally adopted designation, we shall term the molecules of the living matter "plastidules." Molecules, again, are composed of simple elementary atoms, the quantity and nature of which give the essential character to every substance. While the molecules of inorganic bodies are formed by relatively few atoms, we know that the plastidules are much more complicated in their atomistic construction. Every plastidule is constituted by at least five elements, namely: carbon, oxygen, nitrogen, hydrogen, and sulphur. The nature of the union of these elements is a very complicated one in every plastidule, but not as yet elucidated. We generally call the organic substances simply proteinates, or

* "The Cell Doctrine in the Light of Recent Investigations," *New York Medical Journal*, 1877.

albuminates, comprehending by these terms both the living matter and its derivations or products. According to Hoppe-Seyler, the proteinates are composed of: carbon, 51.5 to 54.5 per cent.; oxygen, 20.9 to 23.5 per cent.; nitrogen, 15.2 to 17.0 per cent.; hydrogen, 6.9 to 7.3 per cent.; and sulphur, 0.3 to 2.0 per cent.

Manifestation of Life. While chemical examination has revealed very little of the intimate nature of living matter, we know certain properties to be essential to living matter as long as it is really alive, and we know, also, some of its morphological features, to as great an extent as direct observation is possible with our best modern magnifying apparatus. The physiological properties are visible in every moving and growing organism, and they must be attributed to the minutest living particles as well as to the whole organism. We consider living matter alive only so long as it exhibits to us certain physiological properties; when motion and reproduction cease, it is dead. Life is evidently a peculiar kind of motion of the molecules (plastidules) of living matter, of a relatively short duration. A change of the motion is disease; cessation is death. The chemical changes of living matter are different during life and death; the former are manifested by motion and reproduction, the latter by decomposition, which means simplification of the atomic construction. The shape of living matter is changed by decomposition, but by preservation we succeed in retaining the shape of the substance, which we know was once the seat of life, and microscopic morphology is largely based upon observation of dead but preserved living matter.

Properties of Living Matter. The physiological properties are mainly two: motion and reproduction—viz., the capability of producing its own kind. In speaking of the motion of living matter, we do not mean the motions to which every substance is subject, and of which light, heat, electricity, etc., are peculiar manifestations. There are certain forms of motion dependent on the contractility or irritability of living matter which do not occur in inorganic bodies, nor in organic matter after it has ceased to be alive. This kind of motion enables living matter to work, at least to a certain limited degree, against the law of gravity. It is controlled by complicated laws, which we term the "will" and the "spontaneity" of living matter. According to M. Foster, the term "automatic motion" is preferable to "spontaneous," inasmuch as it does not necessarily carry with it the

idea of irregularity, and bears no reference to a "will." This motion is of two varieties: one leading to changes of shape—*the amœboid motion;* the other to changes of place—*locomotion.* Both kinds are due to a peculiar structure of the living matter in a certain stage of its development, and will occupy us afterward. Here I will only mention that, in former times, locomotion was considered as a characteristic quality of animals. To-day we are aware that a great many of the low forms of vegetable life in different stages of development are endowed with locomotion, apparently depending on a certain degree of individual will.

The property of producing its own kind is exclusively possessed by living matter, and is also of two varieties, viz.: production for the benefit of the individual itself, with the result of increase of size—*growth;* and production of new individuals—*generation.* We know that every living body is originally small; the ovum of the largest animal is just perceptible to the naked eye, but it increases by taking up nourishing material from without—it grows. After having reached a certain size it does not grow larger, but only reproduces, renews the used-up material, until at last it ceases to renew anything, and then becomes what we term dead. To-day, scientists have arrived at the conviction that the building-material of plants cannot be essentially different from that of animals. With advancing knowledge of natural philosophy, the boundaries between the animal and vegetable kingdoms have more and more faded away. It is impossible, in many cases, to say exactly at which point of development an organism is a plant or an animal.

It has been claimed that the only distinguishing character between plants and animals is that the former feed on simple or elementary inorganic material, while the latter take in organized food; but this opinion can hardly be maintained, inasmuch as it is impossible to say how the lowest forms of animals are nourished at all. We know, moreover, through Charles Darwin's researches, that there are carnivorous plants.

Generation. The property of generation may be looked upon, in accordance with E. Haeckel's definition, as a growth of the individual beyond its individual limits; at least, every organism must reach a certain degree of development before it is fit for propagation. It is known that among the lowest forms of organisms propagation takes place without sexual intercourse, whereas there is a division of labor among the higher organisms, both vegetable

and animal; in the former case, one individual gives rise to a new one; in the latter, two individuals (male and female) are required to produce a third. It is known, furthermore, that the simplest form of propagation is division, when one individual, after having increased in size, splits into two organisms of smaller size. A variety of this process is the "gemmation": *e. g.*, a small bud, growing from the surface of the mother-body, becomes gradually pedunculated, and at length separates by breaking of the pedicle, and forms a new individual. Another variety is the "endogenous formation," in which a lump originates and grows within the mother-body, and is freed afterward through bursting or active perforation of the mother. Essentially all these processes are the

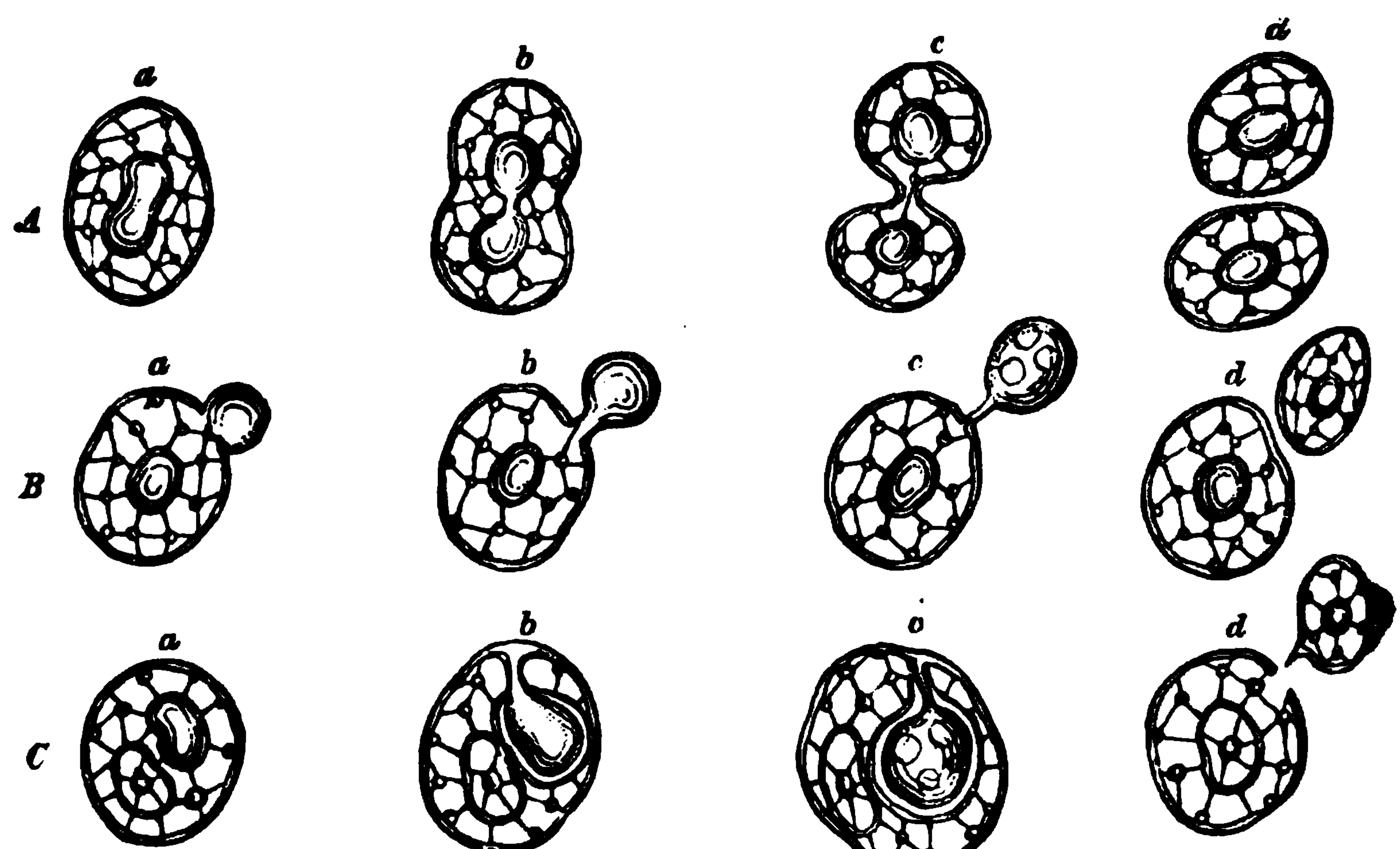

FIG. 1.—DIAGRAM OF GENERATION.

The series A represents simple division. The body at first shows a slight impression on the periphery of the nucleus, *a*; the impression becomes deeper on the nucleus and visible on the body, *b*; the nucleus has separated into two nuclei, and the two halves of the body are connected by a thin pedicle, *c*; two new individuals have been formed by breaking of the pedicle, *d*.

The series B represents the generation by gemmation or exogenous formation. The body projects a solid, homogeneous bud of living matter, *a*; the bud is attached to the mother-body by a broad pedicle, *b*; the bud, by taking into its interior some liquid from without became vacuoled, and is attached to the mother-body by a very thin pedicle, *c*; the pedicle has broken, and two new individuals are formed, the original bud having assumed the structure of the mother-body, *d*.

The series C represents the generation by endogenous formation. The body exhibits by the side of the nucleus a larger lump of living matter, growing from a small granule, *a*; the lump has grown larger and become attached to the wall of the mother-body by a pedicle, at the same time around the lump a space has formed, closed by a flat layer of living matter, *b*; the lump has become enlarged and supplied with vacuoles, *c*; the lump, now of the structure of the mother-body, has escaped through a perforation of the wall of the mother, *d*.

same, and the main form of propagation is always a division. Even in the most highly developed mammals the embryo originally forms a part of the mother-body, and, after having grown, by internal gemmation or endogenous production, up to a certain size, separates from the vehicle, the womb, and represents a new individual. (See Fig. 1.)

Remak was the first to draw attention to the three forms of propagation, but he was not aware of their being materially identical, though morphologically different, manifestations of one and the same process.

There is a striking peculiarity about generation, viz.: the resemblance of the newly formed body to the producing organisms, the parents. It is an easy matter to understand that both individuals will be alike in a case of simple division, because both formerly made one single body; but how shall we explain the remarkable fact that, in higher animals, the offspring so closely resembles the progenitors, though only very minute parts of these—the ovum and the spermatozoids—contributed to give rise to a new individual?

The opinion of E. Hering, that organized matter is endowed universally with an "unconscious memory," a function upon which depends, besides the capacity of imagination, of thinking, of habit, also nutrition and propagation, is not an available one. I therefore take into consideration only the three modern hypotheses of Charles Darwin, Louis Elsberg, and Ernst Haeckel. Darwin promulgated in 1868 the "Provisional Hypothesis of Pangenesis," which consists essentially in the assumption that through all stages of development the living cells or units of the body throw off small granules, or "gemmules," which accumulate to form the sexual elements; and all the cells of the body, therefore, participate indirectly in the new formation of organisms. In 1872, Elsberg published his theory of the "Regeneration or Preservation of the Plastidules." He lays down the proposition that the germ of every living individual contains plastidules of all its ancestors; so that these are bodily regenerated in their offspring, simply because bodily particles are preserved directly from generation to generation. In 1875, Haeckel announced the hypothesis of the "Perigenesis of the Plastidules," according to which, in opposition to the opinions of Darwin and Elsberg, no regeneration or preservation and transmission of plastidules takes place, but only a transmission of motion through inheritance.

Among these theories, I confess that that of Elsberg seems

to me the most probable one, inasmuch as it tries to explain why certain properties of ancestors, even in the second or third generation, may re-appear; why bodily and mental peculiarities are directly transmitted from parents and grandparents to their offspring. With this theory, which suggests a direct increase of plastidules within a limited bulk of living matter, we may readily understand why, with progressive development of a species, a perfection takes place which leads to the production of more and more advanced beings from relatively lower ancestors. Haeckel's view can scarcely be supported so long as we know that a change of motion as function is always due to a material cause, namely, change of molecules in quality and quantity. All this is speculation only, though entirely legitimate as an attempt to bridge over precipices which present insurmountable obstacles to the passage of our intellect.

Historical Sketch of the Study of Living Matter. In 1835, Dujardin discovered a contractile substance common to low animals, which he termed "sarcode," but he was far from the knowledge that this substance exists in all animals, believing it to be peculiar to the lowest forms. After Schleiden, of Jena, in 1838, discovered the form-elements of plants, and proposed for them the name of "cells," Theodor Schwann, of Berlin, in 1839, found a striking analogy between the intimate structure of vegetable and animal organisms, and asserted that the "cells" are the simplest constituent parts of all tissues of the animal body as well as of the plant. In his opinion, each cell is a vesicle composed of a transparent membrane, containing a fluid in which is suspended a central solid body, the nucleus. Schwann believed that cells may originate in a substance, the plasma, independently of former cells, and through the authority of Johannes Müller, who fully accepted Schwann's doctrine, this became the leading one, so that even C. Rokitansky held at first that the plasma of the blood may, under favorable circumstances, produce cells. It was the discovery of Rudolph Virchow, in 1852, that the cells are really the seats of life, and that every cell must originate from a former cell: *Omnis cellula e cellula.* Virchow, however, adhered to Schwann's original idea as to the construction of cells, although a very simple consideration will show that this cannot be correct—viz., the consideration of the fact that no living material is ever a fluid, but always either a solid or a jelly-like, semi-fluid substance. The next who advanced the cell-theory was Max Schultze, of Bonn. He

showed, in 1861, that changes of form, locomotion, and division are impossible to corpuscles surrounded by a resistant membrane; he maintained that the smallest individual elements of organisms are lumps of a jelly-like matter endowed with life, for which he proposed, for good reasons, in accordance with the German botanist, Hugo von Mohl, the term "protoplasm." This jelly-like substance is identical with Dujardin's "sarcode." Max Schultze was the first to announce that the living matter of the infusion-animalcules and that of the cells of all animals are one and the same substance. The cell consists, according to this observer's views, of a minute particle of protoplasm, in which there are imbedded the nucleus and granules. In the same year (1861), E. Brücke, of Vienna, though accepting Max Schultze's views, asserted that the nucleus is not an essential part of the cell, as he knew of many living lumps without any nucleus. Brücke defined the "cell," for which he also proposed the name of "elementary organism," to be a structureless lump of protoplasm; though fully aware of the necessity of the existence of some structure, as in every substance, he regarded the structure of the cell as imperceptible to our senses. S. Stricker, in accordance with Brücke, in 1868, explained that the cell is nothing but a particle of structureless protoplasm, usually containing granules, but that these granules are not essential characteristics. He especially examined the form-elements of the ovula of frogs while studying their development, and observed in these elements hyaline flaps, which he took for pure protoplasm, whereas the greater part of the protoplasm was filled with granules, or particles of yoke. The fact that every living lump is capable of taking in foreign minute corpuscles, granules of carmine or aniline, for instance, from without, led him to the conclusion that protoplasm, perhaps, is devoid of any visible structure, while the visible granules are secondary products of the protoplasm, or foreign substances accidentally taken into the interior of the protoplasmic lump. S. Stricker, in his "Histology," discusses the question, "how large the lump of protoplasm must be to be entitled to the name of 'cell,'" and comes to the conclusion that we should call a living corpuscle a "cell" only when we perceive in it the properties of a living organism—viz., growth, motion, and reproduction. Lionel Beale (1860), independently of Max Schultze's doctrine, announced similar views, arriving, however, at conclusions quite different from those of German biologists. Apparently his microscopes, al-

On some amœbæ during the locomotion the following observations can be made. Most favorable for this study are amœbæ containing a certain number of foreign bodies. The droplet of the infusion should not be taken too large, as a floating amœba changes its shape, but not its place. The creeping begins after the amœba, if little fluid be present, reaches the surface of the covering-glass or the slide.

We notice that in a central portion of the body, near the nucleus, the granules approach each other, slightly increasing in size, and that foreign bodies accidentally present between them are retained. At the periphery of the body corresponding to the contracted portion, a bulging of a pale protrusion takes place simultaneously; in this protrusion a delicate reticulum is, at first, still recognizable. The more the protrusion bulges out, the more it flattens on the surface of the glass, the more does the reticulum fade, until there is left only a light, structureless flap. In a moment, the foreign bodies then rush into the hyaline flap, followed by a floating of the granules of the protoplasm,* and the body of the amœba, including the nucleus, is dragged toward the protruded portion, which, meanwhile, has re-assumed the reticular structure; in other words, the locomotion is accomplished.

In infusions over one week old we find in almost every amœba coarse, shining granules, in varying number. The nucleus of such an amœba, which I briefly call an old one, often, instead of looking homogeneous, contains one or several minute cavities—vacuoles. Such vacuoles sometimes appear in the body of the amœba, too, and each vacuole is seen bounded by a continuous thin layer of a shining substance. Not infrequently, two vacuoles coalesce by the breaking of the thin separating layer, and thus, at first, an hour-glass shaped, later, a roundish cavity, is established. The vacuoles may disappear, as a rule, suddenly, and in their place the reticulum becomes visible, just as in the rest of the body; sometimes within a vacuole, one or more granules are seen in an oscillating motion.

Upon placing a drop of glycerine at the edge of the covering-glass, each amœba contracts into a homogeneous, yellowish, shining, and immovable lump the moment it is reached by the glycerine. Here and there a small vacuole is perceptible in such

* W. Kuehne has already observed the floating of the granules in the amœba. Untersuchungen über das Protoplasma und die Contractilitaet. Leipzig, 1864.

a lump. Some of the lumps remain in the shape described; most of them, however, after a few minutes, gradually resume the granular condition with increase of their circumference; at the same time they become globular and again nucleated. Such an amœba remains motionless.

In still older infusions, amœbæ make their appearance which are characterized by large size, slowness of locomotion, and the property of pushing out radiating offshoots. Such amœbæ are especially sensitive to the action of distilled water. By placing a drop of distilled water at one edge of the covering-glass, and draining off the infusion water from the opposite edge, the following observation was made: Instead of long, radiating offshoots, broad and short flaps were protruded, the long offshoots already present were gradually retracted, and locomotion ceased. Slowly the amœba assumed a blunt, polygonal shape. In its body vacuoles appeared, at first small, gradually larger; the nucleus became indistinct, and afterward completely faded away. Some of the granules, with jerking movement, united into larger groups, while others were seen to float in larger meshes. The more the number of such free granules increased, the more the amœba approached the globular shape. At the same time, many small vacuoles coalesced into a single large one, and a globular protrusion at the periphery of the body resulted. Both the protrusion and the body of the amœba were seen to be inclosed by a continuous shining layer. Within the vacuole, small granules moved about. In the meantime the jerking motion of the grouped granules had ceased, and the number of the floating ones became considerably augmented.

This description of the appearances after addition of water is taken from one amœba; but all amœbæ of the radiating variety, under similar circumstances, exhibited the same features.

Blood-corpuscles of the Craw-fish (Astacus). In a drop of blood, transferred from a broken limb of a living fresh craw-fish upon a slide, and covered with a covering-glass oiled on its edges, we recognize the blood-corpuscles with moderate powers of the microscope. E. Haeckel * found these corpuscles to be amœboid. Two kinds of such corpuscles are noticeable, viz.: pale and finely granular ones with nuclei, which are either large and pale or small and coarsely granular; and, second, others having only coarse, yellowish, very shining granules. The granules of the latter kind, as a rule, encircle light spaces containing scanty granules.

* Ueber die Gewebe des Flusskrebses. Müller's Archiv. 1857.

If at the ordinary temperature of the room we watch a pale corpuscle, we recognize light offshoots slowly changing their shapes, which protrude from the periphery of the corpuscle, while the groups of the granules in the protoplasm are also changing their shape and location. The latter changes consist in an alternating accumulation and separation of the granules, or their transformation into a delicate reticulum.

Almost every coarsely granular body shows under a high amplification the following, in the course of from half to one hour: Each single granule at first represents a globular, yellowish, very shining body, which is separated from its neighboring granules by a light, narrow rim, and this rim is traversed by rather indistinct delicate spokes, connecting each granule with all its neighbors. Each granule continually changes its location, the more noticeably the greater the distances between the single granules. At the same time, hyaline flaps begin to protrude from the periphery of the granular blood-corpuscle. Soon each granule becomes flattened, cup-shaped, and all of them are now seen distinctly connected by gray spokes. Meanwhile the circumference of the whole body has enlarged. Next, in every single granule there appear one central or two excentric vacuoles, which by enlarging and coalescing hollow out the granule so as to make it look like a single or double shell, or ring. Two or more hollow granules suddenly coalesce and are transformed into a delicate reticulum, to such an extent that in place of the former coarse granules a pale, finely granular protoplasm has made its appearance. Inside of it a hollow body becomes visible, inclosed by a relatively thick and scolloped shell, and containing several coarse granules. Such a body, in accordance with our usual terminology, must be called a nucleus.

The pale protoplasmic bodies come from coarsely granular ones, continue for a time to change their shape; the nucleus and its granules (the nucleoli), on the contrary, from the moment they have appeared, do not change.

Upon adding a one-half per cent. solution of chloride of gold to a fresh specimen of blood, the liquid was transformed into a finely granular coagulum. The pale protoplasmic bodies had become globular, and the coarsely granular transformed into many-shaped masses, having in their interior a delicate reticulum surrounded by a continuous layer. In both kinds the nuclei remained coarsely granular and coarsely reticular. After one hour, the solution of gold being drained off, and the specimen

exposed to daylight, the yellow, shining substance which produces the reticulum in the protoplasm and its nucleus assumed a violet color, while the substance within the meshes remained uncolored. *

Blood of the Newt (Triton). In a drop of blood of the newt, transferred to the glass slide and covered with a covering-glass oiled on its edges, we can observe the motion of the colorless blood-corpuscles for hours at the temperature of the room. The changes of shape result from a protrusion of light flaps and granular offshoots of varying breadth, and sometimes of considerable length, from the periphery of the protoplasmic body.

Many finely granular bodies exhibit in their interior a continuous change of the grouping of the granules. Especially after addition of a one-half per cent. solution of chloride of sodium, during the locomotions of the body, vacuoles arise, and the inner surface of the wall of many vacuoles looks jagged, as if beset with torn points. For moments the whole body is vacuoled, the smallest, just perceptible, vacuoles being transitions to still smaller meshes, the filaments of which show pale gray granules as points of intersection; this appearance is only temporary, as the next moment most, or even all, of the vacuoles may have disappeared.

In fresh blood, some coarsely granular colorless blood-corpuscles distinctly show filaments emanating from the granules. With the assistance of an immersion-lens, No. 15 of Hartnack, I became convinced that, during the locomotion of the corpuscle, the single granules continually keep changing their size and shape, as well as their location.

In the blood of newts which had been kept all winter, the nuclei of many colored blood-corpuscles were visible, both immediately after the mounting of the specimen and after it had remained a time on the glass slide. Each nucleus exhibits a number of coarse, very shining granules, some of which show filaments that are united with the neighboring granules. The nucleus is bordered by a continuous layer of a substance of the same refraction and color as the granules. There is often seen around the nucleus a very narrow light rim, which at times

* According to N. Lieberkühn (Ueber Bewegungserscheinungen der Zellen, 1870), in blood-corpuscles of many caterpillars there exists a space between the contractile layer and the nucleus which is traversed by filaments extending from the inner surface of the contractile layer to the outer surface of the nucleus.

looks traversed by delicate radiating spokes, lost to sight in the colored portion of the blood-corpuscle.

The specimen shows numerous free bodies of the aspect of nuclei of red blood-corpuscles, and the surface of many of such bodies is beset with pointed, as if irregularly torn, filaments. Besides, there are globular bodies in smaller number, which decidedly surpass the size of these, though they are coarsely granular, and inclosed by a shell, like the nuclei. Neither of these formations exhibited locomotion at the ordinary temperature of the room.

Colorless Blood-Corpuscles of Man. I have transferred to the heating stage my own blood, which I took from a small prick of the palmar surface of the thumb. No structure was recognizable in the shining colorless corpuscles at the temperature of the room. As soon, however, as the temperature of the specimen reached about 30 deg. C. (86 deg. F.), the colorless blood-corpuscles—I mean the finely granular ones, resting in plasma encircled by red blood-corpuscles—always exhibited the following features:

In the center of the corpuscle one or two gray, opaque, homogeneous lumps made their appearance. From every lump emanate radiating conical spokes, which unite the two lumps, when such exist, or which are directed toward the periphery of the body and inosculate with a net-work traversing the whole corpuscle—a net-work the points of intersection of which appear slightly thickened, in the shape of nodules, or granules. On the periphery of the corpuscle the reticulum is inclosed by an apparently continuous, somewhat shining, layer. The central lump, the spokes, and their nodules are identical in their optical features, while the mesh-spaces give the impression of light, structureless fields. (See Fig. 2.)

FIG. 2.—DIAGRAM OF A LIVING COLORLESS BLOOD-CORPUSCLE.

As the temperature of the specimen rises gradually toward 35 deg. C. (98 deg. F.), continuous changes of shape occur, both in the central lump and in the net-work of the corpuscle. Simultaneously with changes of the shape of the latter, a smaller or greater portion of the central body at times is transformed into a reticulum,

while, in the rest of the corpuscle, coarser groups of granules arise, with either no mesh-spaces or else very narrow ones. The groups at times are dissolved, and re-appear in different places, and such alternations continue even when the temperature is gradually lowered.

In one colorless blood-corpuscle (temperature 23.5 deg. C., 73.6 deg. F.), a vacuole made its appearance, in which a torn granule oscillated. I observed that the granule changed its shape, and, at its periphery, delicate filaments appeared and disappeared. On one occasion, three unusually long filaments were thrown out so as to reach the wall of the vacuole, whereupon the vacuole suddenly disappeared. Afterward, a new vacuole, containing a granule, presented itself in nearly the same place; but this vacuole became dumb-bell shaped and enlarged by the rupture of the wall of a neighboring vacuole. Still later, the whole blood-corpuscle was transmuted into a vacuoled lump, which continued to change its shape, though very slowly. (See Fig. 3.)

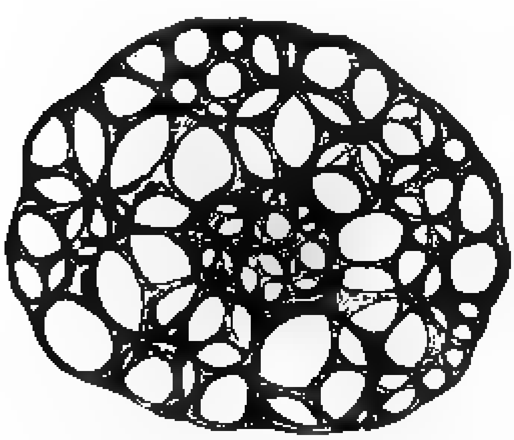

FIG. 3.—DIAGRAM OF A VACUOLED BLOOD-CORPUSCLE.

In some blood-corpuscles, small, vesicular nuclei, with dark contours, and constantly one or two nucleoli, often arose at an ascending temperature below 30 deg. C. (86 deg. F.). Such nuclei, on raising the temperature, originated in different places of the corpuscle, as I could directly observe, from pale gray, compact lumps, devoid of a dark contour. In addition to the larger, distinctly bordered nuclei, up to the number of four, I also met with a varying number of smaller nuclei. The nucleoli within a dark-contoured nucleus possess delicate radiating spokes, which go to the boundary layer of the nucleus. The boundary layer, invariably surrounded by a light rim, sends off numerous spokes, and these inosculate with a network traversing the whole corpuscle. (See Fig. 4.)

FIG. 4.—DIAGRAM OF A DEAD BLOOD-CORPUSCLE.

Blood-corpuscles in which nuclei of the above description had originated, did not materially change their shape, even if the temperature was raised up to 35 deg. C. (91 deg. F.); the only noticeable change consisted in a temporary bulging from the periphery of the corpuscle, of a hyaline flap which slowly increased in size. In such a flap, no structure was perceptible, but sometimes very small vacuoles, which were invariably inclosed by a somewhat denser, slightly shining substance.

Colostrum Corpuscles. The colostrum, as is well known, holds a variable number of protoplasmic lumps, which sometimes contain fat-granules, and, as first demonstrated by S. Stricker,* upon raising the temperature up to 40 deg. C. (104 deg. F.), change their shape and location—therefore are alive. If we look, with an amplification of an immersion-lens, No. 15 of Hartnack, at a pale lump ever so small, which, with lower powers appears to be structureless, we find in every one of them, even though a nucleus be wanting, a reticulum identical with that of a colorless blood-corpuscle. The points of intersection of the reticulum are granules, either very small and pale gray, or somewhat larger and glistening. Some granules exhibit the peculiar luster of fat, but are in connection with the rest of the corpuscle by means of delicate filaments. Larger droplets of fat apparently lie isolated in the mesh-spaces. The author named has proved that granules of fat may be discharged from the protoplasma during its contractions.

In the foregoing, I have collected a number of facts, observable by every one who has a well-versed eye and a good lens. I now proceed to draw conclusions from my observations.

First, it is obvious that a reticulum in protoplasm, as conceived but not seen by E. Brücke† and S. Stricker,‡ is visible. The protoplasm, therefore, is not structureless, but has a reticular structure, and the granules are not foreign, but belong to living protoplasm, being the points of intersection of the reticulum.

The Nucleolus, the Nucleus, and the Granules, with their Con-

* Ueber contractile Körper in der Milch der Wöchnerin. Sitzungsber. der Wiener Akad. d. Wissensch. 1866.

† Ueber die sog. Molecularbewegung in thierischen Zellen, insonderheit in den Speichelkörperchen. Sitzungsber. d. Wiener Akad. d. Wissensch. 1863.

‡ Untersuchungen über das Leben der farblosen Blutkörperchen des Menschen. Sitzungsber. d. Wiener Akad. d Wissensch. 1867.

necting Filaments, are the Living, or Contractile Matter Proper. This solid matter is suspended in a non-living, not contractile liquid. In other words, *the contractile matter in mesh-spaces contains and, as a shell, incloses, a non-contractile fluid matter*, which latter cannot be simple water, as the phenomena of diffusion prove.

Starting from the *condition of rest* of the protoplasma as it appears in a colorless blood-corpuscle which has just become dead, we may consider every granule as a central portion of contractile matter, which connects with that of its neighbors by means of narrow bridges. (See Fig. 5.)

A

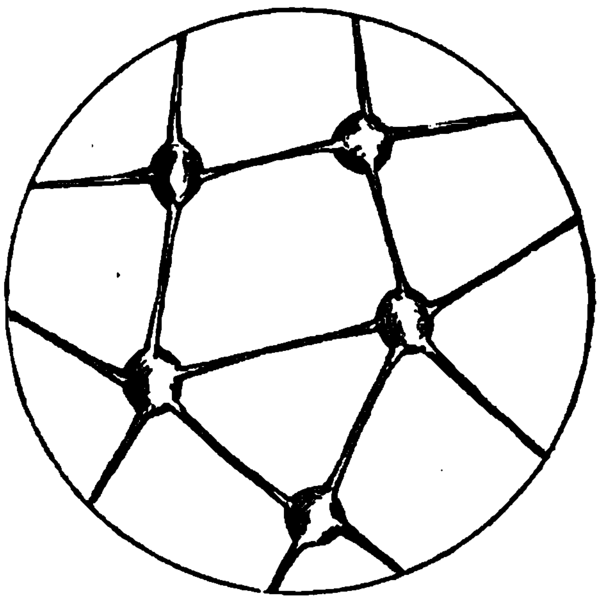

FIG. 5.—DIAGRAM OF REST.

Contraction consists in an increase of the size of the granules, and their approachment to each other. Hereby the filaments are obviously shortened for the benefit of the granules. (See Fig. 6.)

Tetanus I will term the condition which I observed in amœbæ brought in contact with glycerine. It is caused by an intense contraction of the living matter. (See Fig. 7.)

B

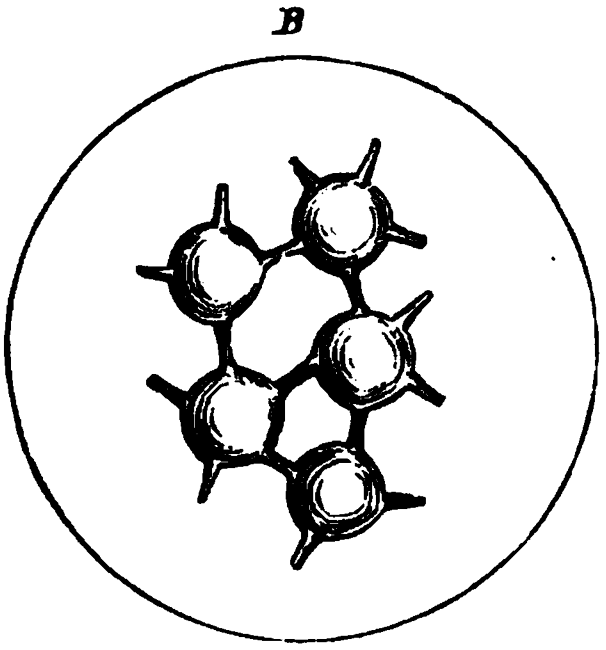

FIG. 6.—DIAGRAM OF CONTRACTION.

C

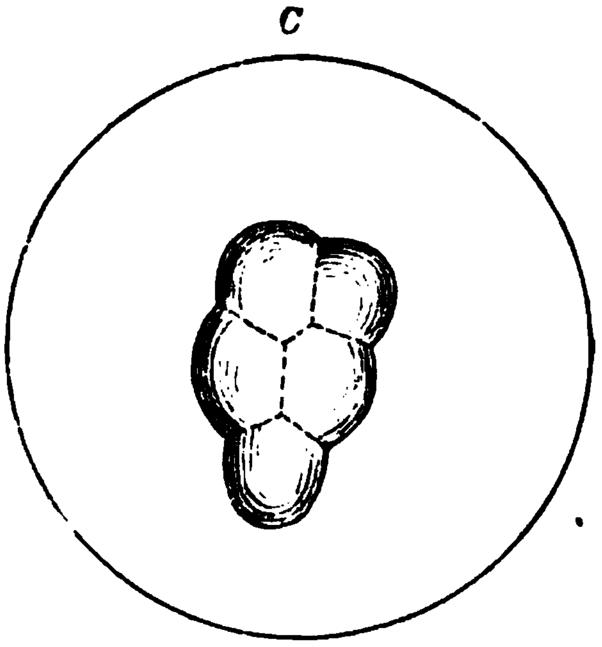

FIG. 7.—DIAGRAM OF TETANUS.

Extension, on the contrary, consists in a decrease of the size of the granules until they almost disappear, with their simultaneous moving apart, and an elongation of the filaments at their expense to apparent fading of the structure, as in the hyaline flaps. (See Fig. 8.)

In addition to these differences in the shape of living matter, I would mention the *swelled globule* (Quellungskugel). This shape occurs under the influence of a liquid less concentrated than that held in the protoplasma, as, for instance, on addition of distilled water. Some authors have considered this as the condition of rest. It is preceded by a jerking of some groups of granules, without change of the general shape of the protoplasmic body. At the same time many granules are torn asunder, and float about in the mesh-spaces, which have become enlarged by numerous ruptures.

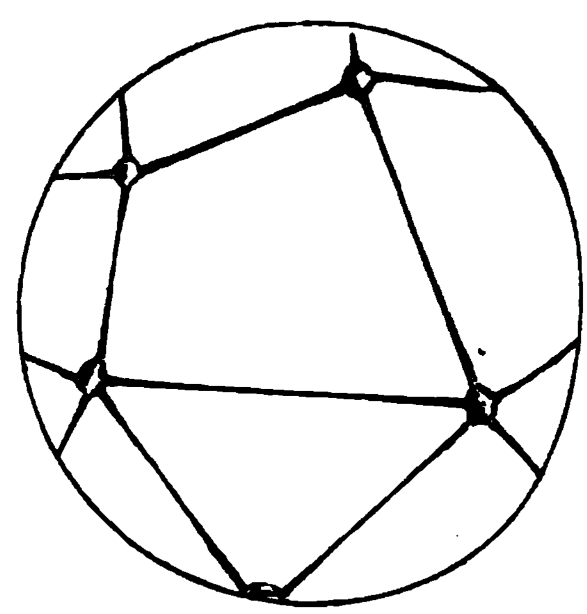

FIG. 8.—DIAGRAM OF EXTENSION.

Increase of the liquid in the protoplasm is accompanied by the *formation of vacuoles*. In the liquid contained in the vacuole, granules torn off float about, and may throw out filaments; these filaments may extend so far as to reach the wall of the vacuole. In such a case the latter instantaneously disappears, and the former condition of the net-work is reëstablished.

Should the wall of a vacuole near the surface break in consequence of an increasing tension, or that of the protoplasmic body itself break, the protoplasmic liquid will escape in the first instance; while in the second, a piece of the protoplasmic body may be torn off, the *débris* of which, to the minutest granule, are still viable. Or the whole reticulum may break down, and the surrounding liquid, water, not favoring the life of the contractile matter, deprives every particle of its life.

ANALYSIS OF THE ASSERTIONS MADE IN 1873.

The reticulum in the "protoplasm" was seen and depicted by Nasmyth (1839), in corpuscles which to-day are known to be the covering epithelia of the tooth; by C. Frommann (1867) in "ganglion-cells," and by others in the same and other corpuscles. What I have described, is a reticular structure of the "protoplasm" as a universal occurrence, and my assertions have since been corroborated by all good observers.

In 1877, I added the following remarks: *

* "The Cell Doctrine in the Light of Recent Investigations," *New York Medical Journal*, 1877.

"The fully developed protoplasmic body is constructed like a sponge, but, at the same time, inclosed on all sides by the same substance which forms the trabeculæ of the sponge—the trabeculæ and the shell being the living matter.

"An analysis of the observations of the living protoplasmic body teaches us that there can be distinguished mainly three different appearances of the net-like living matter—namely, that of rest, that of active contraction, and that of passive extension.

"In the state of rest, as seen in a motionless amœba, or immediately after death, the granules are almost uniformly distributed throughout the protoplasm, united with each other by slender threads, the bridges of living matter.

"In contraction, we observe an enlargement of the granules by shortening of their uniting threads and approximation to each other. Nothing has been added to the living matter and nothing lost from it; only the distribution of the plastidules has changed, leading to the narrowing of the net-work, and a partial expulsion of the fluid formerly contained in its meshes. Contraction is the active property of living matter, and on it are based the simple change of shape and the locomotion of the whole organism.

"Extension depends upon a decrease of size of the granules, with a removal from each other and an elongation of the uniting threads at the expense of the bulk of the granules, even to the disappearance of all structure. The extension takes place in a passive manner; the fluid contained in the meshes of the living matter is pushed out toward the periphery, and there leads to the formation of a protruding offshoot—the hyaline flap. At the beginning of the protrusion we still observe in the flap the presence of structure, while at the highest point of extension the structure can no longer be seen, because granules and threads have been elongated to their utmost capability. We may compare this phenomenon to the extension of glass rods, melted on a flame until the threads become so thin as to disappear to the naked eye.

"These three states of living matter explain to us not only the movement of a simple protoplasmic lump, but also the action of the most highly developed muscles, which, as I have demonstrated, are entirely identical in their structure with the simple amœba. Were the amœba a sponge without an inclosing layer of living matter on its surface, every contraction would lead to an escape of the fluid, and no locomotion would be possible; the presence of an outer, although very thin, layer of living matter is necessary to the various movements of living protoplasmic bodies.

"By adding a drop of glycerine to the creeping amœba, or to any protoplasmic body, we can bring about a fourth state of living matter, viz., the highest degree of contraction, for which S. Stricker and I have proposed the term 'tetanus.' The fluid of the protoplasm being suddenly extracted by the glycerine, all granules flow together, forming a structureless lump of much smaller size than that of the original corpuscle, without visible limits of the single granules. A rehabilitation of the former net-like structure is produced by taking away the glycerine and adding water, without reëstablishment of motion.

"All these changes of living matter can be directly seen under the microscope. But we cannot observe the formation of a flat, extended layer

at the boundaries of the whole body, at those of a hollow nucleus and of every vacuole. I therefore had to have recourse to the hypothesis that a granule may send out offshoots in great number, leading to the disappearance of the central mass, and that these offshoots, melted together, may produce a continuous layer. By the union of many such areas an extensive layer could be produced, large enough to cover in the whole protoplasmic body. (See Fig. 9.)

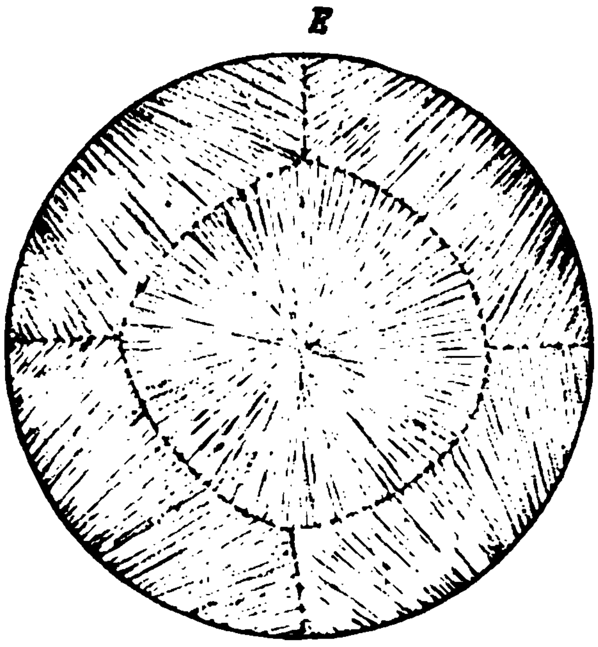

FIG. 9.—DIAGRAM OF THE FLAT LAYER.

"The presence of a layer of living substance on the outer surface of the body explains to us why every protoplasmic lump can so easily take up foreign bodies, and why vacuoles can form and disappear almost suddenly. We must imagine that the living matter is capable of entering any of the described states at any time, so that a flat layer, for instance, may immediately change into a net-work, and *vice versâ*. When the lump swells up through the addition of water, the granules are torn apart and float freely in the fluid, as occurs in swelled amœbæ and saliva-corpuscles. The breaking of the outer shell, with escape of minute particles of the amœba, still endowed with life, and the process of the division, can also easily be understood. . . .

"In conclusion, I may draw attention to the fact that the amount of living matter varies greatly within a limited bulk of protoplasm, both in normal and morbid conditions. The colorless blood-corpuscles of persons exhibiting signs of lymphatic, strumous, scrofulous constitution, contain much less living matter than those of strong, vigorous persons. Further examinations will in all probability teach us to make use of these differences for practical purposes. I announced three years ago that the protoplasmic lumps forming tubercle are characterized by a relatively small amount of living matter. Last year I published my observations on pus-corpuscles, which enable me, from the relative amount of living matter contained in an individual corpuscle, to say from what kind of organism such a pus-corpuscle is formed; whether the person from whom the pus comes is healthy and strong, or weakened by chronic disease, as tuberculosis."

The idea of a structureless protoplasm was little satisfactory. Since 1873 this structure is known to be reticular, though the reticulum itself, with all its nodulations, allows of no further discrimination of structure. How complicated the reticular or filamentary structure of the nucleus may be, is brought to evidence by the researches of Auerbach, Flemming, E. Van Beneden, O. Hertwig, and others. The radiating "suns" as they appear in the process of division of the nucleus, the "Karyokinesis" of Flemming, become explicable by the presence of a substance able to grow, to move, and to assume different shapes.

Only a Part of Protoplasm is Living Matter. The main stress to be laid on my assertion that not the whole mass hitherto rmed protoplasm is endowed with properties of life, but only part of it—the living matter proper. As I shall later on emonstrate, the living matter appears first in the shape of a lid, homogeneous, apparently structureless granule, which by rowing, by taking in liquid, and by splitting into a reticulum, ecomes what has been termed protoplasm. *Protoplasm,* there- ore, *is only one stage in the development of living matter,* and by no means its exclusive appearance under the microscope.

The two main properties of living matter, motion and growth, are possessed by every, even the smallest, lump of living matter. The motion is relatively little marked in a solid lump, and becomes the more evident the more the living lump has split up into a reticulum, the more it has assumed the appearance of "protoplasm." Growth, on the contrary, is a marked property of every granule of living matter; on the increase of its size depends generation, formation of complicated organs and organisms, and new formation, so striking in inflammation and in tumors. All varieties of generation (see page 16) are due to a motion and growth of the living matter, while the protoplasmic liquid, probably nitrogenous too, a substance of secondary formation, is a carrier of nutritive and used-up material of the living matter. The formation of basis and cement substance, and the process of secretion, furnish direct proofs of the significance of the protoplasmic liquid.

Chemical Re-agents. Very little is known as to chemical tests of living matter. Carmine solutions, as a rule, stain it, and this explains why the nucleus, which holds a good deal more living matter than the rest of protoplasm, is more deeply stained; the action of hæmatoxylon (in alcohol specimens) is similar; chloride of gold renders living matter violet; but neither are absolutely reliable. Acids destroy living matter; consequently also acetic acid. The former method of bringing to view the nucleus by treatment with acetic acid simply destroyed the rest, due to the fact that the bulky formations of the nucleus resist the action of acetic acid more than the scattered formations in the protoplasm. This re-agent has scarcely any value. The different stainings of tissues by re-agents, especially combinations of indigo, picric acid, and aniline colors, are caused by a difference of the chemical products of living matter, rather than by a difference of the living matter itself.

Analysis of Rest. Living matter, as long as it is alive, can never be at absolute rest, and in the protoplasm a uniform distribution of the reticulum is not observable as long as motion is present. The condition of comparative rest (Fig. 2) may be exhibited by a portion of the protoplasm; while another portion is in the condition of contraction, another again is in that of extension. Rest is death, and seen in motionless blood or pus corpuscles, which on dying often assume the globular shape—viz., an accomplished equilibrium of the reticulum. By evaporation of the liquid, even such globular bodies may present a jagged, irregular shape, which is not amœboid, as erroneously has been asserted, but the result of shrinkage. Death, however, may ensue at any moment during contraction or extension, if the living matter be killed instantaneously by a re-agent. Motionless pus-corpuscles—f. i., in urine—may be found in greatly varying amœboid shapes, and the peculiarities of the reticulum in the contracted and extended condition remain fixed in such corpuscles if kept in preserving fluids—f. i., solution of chromic acid.

Analysis of Contraction and Extension. Contraction of the reticulum causes the amœboid motion and the locomotion of a protoplasmic mass. The liquid held in the meshes, being driven out of the contracted portion, will rush into a portion at the time at rest, and will extend this portion in the shape of what has been termed pseudopodia. If contraction takes place in one half of the protoplasmic mass, the other half will be in extension; if two peripheral segments be contracted, the intermediate portion will be extended. The latter was suggested by Hermann, long before the structure of protoplasm was known. In the former instance a flap will protrude, nearly of the diameter of the body itself; in the latter a narrow offshoot, a "pseudopodium," will make its appearance, varying in length, and exhibiting either an indistinct structure or being apparently devoid of structure, on account of the great stretching of the reticulum. To allow locomotion to be accomplished, the protruded flap must adhere to a solid base, so as to have a point of fixation, toward which the balance of the body is dragged. An amœba, a colorless blood-corpuscle, can commence creeping only after one of the protruded flaps has reached the upper surface of the slide or the lower surface of the covering-glass, for the same reason that a man can make a step only on a solid ground, and climb only by attaching himself with arms or legs to a support. The motion of protoplasmic lumps is liveliest if the slide and cover be close

to each other, and the intervening layer of liquid, therefore, very small.

Analysis of Tetanus. Tetanic contraction was first observed by S. Stricker, in colorless blood-corpuscles in lively motion, the slide and covering-glass being closely attached to each other, at the moment when the cover was lifted a little by the addition of an indifferent liquid to the edge of the specimen. As soon as the liquid evaporated, motion and locomotion set in once more. I have produced the same condition by the addition of glycerine. Tetanus is also observed in most of the colorless blood-corpuscles and amœbæ, immediately after their transportation to the slide, evidently due to mechanical shock. Similar results were yielded by the electric current. To call such a condition "rest," is certainly erroneous.

Analysis of Investing Layers. The production of a continuous layer of living matter around the protoplasmic mass and a hollow nucleus can be explained by a hypothesis only (Fig. 9). Such a layer is far from being an investing membrane, in the sense of the old cell theory; it is identical in every respect with the reticulum present within the protoplasm. Its capacity of admitting extension is surprisingly great. The thicker this wall is, either around the nucleus or around the protoplasm, the less is the capacity of producing amœboid motion or locomotion. Solid nuclei and nuclei with a broad investing shell do not themselves move, but are carried along in a mechanical, passive way by the moving reticulum around. Coarsely granular protoplasmic bodies with a very marked investing layer do not move. The finer the reticulum, respecting its points of intersection, and the thinner the covering layer of living matter, the more pronounced is the capacity of amœboid motion and locomotion.

The continuous layer of living matter may at any time and almost instantaneously be transformed into a reticulum. A foreign body may be taken into the interior of a protoplasmic body by offshoots embracing the foreign mass, the distal ends of the offshoots then coalescing, and lastly at the proximal ends, the investing layer being converted into a reticulum. The thinner a flat layer, or the more it is stretched, the more prone is it to fuse together with neighboring formations of the same kind. Long offshoots of amœbæ, f. i., easily coalesce to form a coarse reticulum. Not all foreign bodies that are taken into the interior of the amœba can serve as a pabulum, as, f. i., carmine or aniline granules, silicious shells of diatomes, etc.

The bursting of the outer investing layer is necessary for the extrusion of foreign bodies, or fat-granules, or a liquid. Such a wound at the periphery of the protoplasmic body may heal imme-

diately by coalescence of the flat layer. Obviously, the bursting must be due to a sudden and intense contraction of the reticulum close behind, and as the foreign particles are often driven out with a certain force, like a shot, we may conclude that, together with the foreign body, also a certain amount of liquid has escaped from the interior. A momentary reëstablishment of comparative rest in the contracted portion would seem to be required for the coalescence of the separated portions of the outer flat layer. A part of the reticulum itself may penetrate the investing layer, or a single granule with adhering filament. The result will be a small protrusion, or a single granule attached to the outer surface by a slender pedicle.

Analysis of Vacuoles. A vacuole is a lake in the middle of the protoplasmic body, inclosed by a continuous layer of living matter. Without such an investing wall the lake could not be formed. The vacuole may increase in size, either by stretching of the encircling layer, or by confluence with a neighboring vacuole, if the wall between the two should break. The vacuole may suddenly appear, and also suddenly disappear. Granules of living matter are sometimes floating in the lake; sometimes offshoots of a granule reach the inner surface of the wall of the vacuole, and the reticular structure is immediately reëstablished. Vacuoles may be formed, and may disappear suddenly, in ways and for reasons which we do not understand as yet. Formerly, the vacuoles were thought to be stomachs of the protoplasm, an assumption for which we have no ground whatever. Embryological research, on the contrary, proves that vacuoles are elementary vascular organs, containing plasma; as E. Klein first demonstrated, the heart and the blood-vessels are originally nothing else but vacuoles.

Comparison of Amœba and Man. The analysis of a single protoplasmic lump is of the greatest importance, inasmuch as such a lump is the simplest animal organism, on the plan of which are built up all, even the most complicated organisms. It will be demonstrated farther on that the human body is constructed on the plan of an amœba, and the comparison will be carried out in all details. Man is a complex amœba with permanent protrusions, the extremities, with a wonderfully complicated division of labor of the groups of the living matter. Man, in *toto*, is an individual, as is the amœba, and in both, isolated lumps of living matter float about—in the one case in vacuoles, in the other in the blood and lymph vessels.

The Structure of the Blood-Corpuscles of the Oyster.
By A. M. Hurlbutt.*

If we break the shell of an entirely fresh oyster on its thinnest edge, a small quantity of sea-water will ooze out. If we open the oyster by pulling apart the two valves, around the injured oyster a large quantity of fluid accumulates. This fluid contains the blood-corpuscles. First we oil the edges of an extremely thin cover on one side, place a small drop of the juice of the oyster upon a slide, and cover it with the covering-glass, the greased edges looking toward the slide. We then have a specimen ready for examination with the highest powers of the microscope.

A power of about five hundred diameters will reveal numerous granules floating in the fluid, in what has been termed molecular motion. These are granules of fat, of pigment, and of broken protoplasm. In the fluid there are swimming very often parasites, which I do not wish to consider at this time. Furthermore, *débris* of the tissues of the oyster and epithelia are to be seen, and lastly, numerous granular bodies, varying considerably in size and form, and continually changing their shape or locality for at least two hours. These are the blood-corpuscles of the oyster. Let us now put on a lens with a magnifying power of twelve hundred. I used an immersion-lens of Tolles, of Boston, and one of C. Vérick, of Paris, both magnifying about twelve hundred diameters with a short eye-piece, and both giving the same results as to the structure of the protoplasmic bodies.

We find globular bodies of the size of human red blood-corpuscles to be considered as free nuclei, suspended in the fluid, and of which nuclei it is impossible to say whether they exist as such in the live oyster, or are freed by the injuring manipulation. Besides, spindle-shaped bodies are present, not surpassing the nuclei in size. Lastly, protoplasmic bodies are visible, varying in size from one and a half to seven or eight diameters of a human red blood-corpuscle, partly roundish, partly elongated in one or several directions, or stellate,—that is, provided with a number of delicate radiating offshoots. These protoplasmic bodies are in amœboid motion, changing their shape continuously by projecting flaps or elongated offshoots—the so-called pseudopodia—on different parts of their peripheries, and withdrawing them again. The changes of shape are not very lively—about as slow in character as we observe them on the amœba diffluens, or in colorless blood-corpuscles of the newt. At the same time locomotion of the protoplasmic bodies takes place, so that a corpuscle might migrate through the field of vision of the microscope within one hour. On the free nuclei I did not observe changes of shape or locomotion.

The blood-corpuscles are either devoid of a nucleus, or during the observation there may appear roundish bodies within the protoplasm, looking like nuclei and disappearing again from our view. Other corpuscles from the very beginning show from one to five or six nuclei. When nuclei are thus visible at the beginning of the observation, they remain unchanged until the corpuscles in which they exist become motionless. In corpuscles in which no constant nucleus can be made out, sometimes a nucleus becomes visible when the corpuscle approaches the time of its death—that is, when it becomes motionless.

Let us now watch a corpuscle in which a nucleus is plainly marked, and

* *New York Medical Journal*, January, 1879.

we shall see as follows: The nucleus is surrounded by a yellowish shining shell, which either is uniform in its width or looks beaded, as if built up by a number of granules, which are connected with each other by a thinner layer of the same substance of which they themselves are composed. Within the nucleus we again find granules, either uniform in size or some appearing to be considerably larger than others; these latter bear the name of nucleoli. The granules vary greatly in number, and are either scattered irregularly throughout the nucleus or are arranged in the shape of wreaths, concentrical with the outer shell of the nucleus. Sometimes two or even three of such wreaths are to be observed within the nucleus, a fact to which Th. Eimer first drew attention. In small nuclei we observe sometimes only one central granule (nucleolus), and from this granule there project fine threads, from three to six in number, conical in shape, the bases of the cones arising from the granules, their thin ends tending toward the wall of the nucleus, with which all the cone-like threads are invariably in direct union. Thus a wheel-like figure is constructed, the hub of which is represented by the central granule (nucleolus), the spokes by the conical threads, and the felloes by the shell or outer layer of the nucleus, the latter representing only the optical section of the surrounding layer of the spheroidal body. All the described formations are suspended in a pale, colorless, and structureless substance, between which and the fluid part of the blood outside the corpuscles no distinction can be drawn. When there are several granules present in the nucleus, all are joined together by means of fine, grayish threads, the granules thus representing the points of intersection of a net-work which traverses the whole interior of the nucleus. The granules next to the wall of the nucleus—it is immaterial whether regularly or irregularly placed—send delicate grayish threads toward the wall of the nucleus, with which they inosculate. The meshes of the net-work within the nucleus, filled with the homogeneous colorless substance, vary in size. I, however, was not able to decide whether, during the motions of the whole corpuscle, there were also changes in the shape of the net-work of the nucleus, which S. Stricker asserts he has noticed in the net-work of the nuclei of the colorless blood-corpuscles of the frog and newt.

The structure of the nuclei, as just described, is visible on all nuclei, no matter how many may be seen within a protoplasmic body, and also on bodies floating in the fluid specimen which were described before as free nuclei. In none of the latter could I ever discover changes of shape or active locomotion. Not very rarely, however, we meet with small nuclei in the blood-corpuscles, which look almost homogeneous and of a pale, grayish-yellow color, apparently devoid of structure. Such nuclei, which we might consider as somewhat larger granules, are also suspended in the outside fluid part of the blood, as well as in the protoplasmic bodies.

Whenever a nucleus is to be seen in a protoplasmic body, outside its shell a light seam can be observed, always traversed by conical, radiating threads, which spring by their broad bases from the shell of the nucleus, and unite by their thin ends with the granules next to the light seam. Such conical offshoots arise also from compact nuclei, thus giving them the appearance of angular bodies. Throughout the whole protoplasm granules of different sizes are scattered, all of which show the same color and the same power of refracting the light as those within the nuclei. These granules are united with each other by slender threads in the same manner as those in the nuclei. Very

often the appearance is presented of a single granule surrounded by wreaths of other granules, all the latter being united, by means of radiating conical threads, both to the central granule and to each other. Such small, wheel-like bodies may arise in different places in the protoplasmic body during its changes of shape. Besides the grayish-yellow granules, there are numerous others of a more yellow color and of a greater refracting power, identical with that of fat-granules. Experience shows that such fat-granules are more numerous in the latter part of the breeding season of the oyster—viz., in July and August. Many of these fat-granules are connected by means of delicate threads with the neighboring protoplasmic granules.

During the changes of shape of the blood-corpuscle, round spaces often appear in the protoplasmic bodies, the so-called vacuoles. These vacuoles vary greatly in size; they are filled with the light, structureless fluid substance which we see within and without the meshes of the net-work. In the fluid of the vacuoles sometimes there are granules floating about. Each vacuole is surrounded by an extremely thin grayish-yellow layer, which is always in union, by means of delicate threads, with the neighboring granules of the protoplasm. Sometimes several vacuoles arise within the corpuscle, and are separated from each other by a continuous layer, like the shells of a nucleus, and these shells give the appearance of a frame-work. The same appearance of vacuoles, though on a considerably smaller scale, I have repeatedly observed also on nuclei originally homogeneous and structureless-looking.

A continuous, though extremely thin, layer can be seen on the periphery of and closing in the protoplasmic body. The outer surface of this layer looks smooth, while its inner surface is in connection with the neighboring granules by means of delicate threads.

While we watch a blood-corpuscle of the oyster at the common temperature of the room, continuous changes of its shape are visible, as mentioned above. At the same time, changes of the net-work within take place. Temporarily, the granules seem grouped together and the meshes considerably narrowed; opposite to such a group of closely packed granules flaps bulge out from the periphery of the protoplasmic body. Within a flap there is faintly visible a net-work only at the beginning of its protrusion; very soon this net-work is completely lost to sight, and the flap looks homogeneous, and apparently structureless. At other times, delicate narrow hyaline offshoots are projected from the periphery of the blood-corpuscle, varying in number, and sometimes considerably surpassing in length the diameter of the protoplasmic body. These so-called false legs (pseudopodia), as a rule, look homogeneous, and run either in a straight direction or are curved and repeatedly bent. They are being projected and withdrawn frequently during the changes of shape of the corpuscle; sometimes they are thrown out so regularly, and in so great a number, that the corpuscle assumes a beautiful star-shape, the central body at this time being considerably decreased in size and its granules closely packed together. The offshoots may also be irregular, and the blood-corpuscle may take on a considerably elongated, irregularly angular, and branching shape. On the thicker parts of the offshoots the net-like structure of the protoplasm is to be seen, while their ends always look hyaline and structureless.

During the changes of shape, sometimes a number of granules melt together, thus producing the appearance of a temporary nucleus; such a

nucleus, after a few minutes, may disappear again, and a net-work be reëstablished, where shortly before there was a compact lump. Sometimes round bodies looking like nuclei jump forth from the interior of the blood-corpuscle, and float freely in the surrounding fluid. Sometimes protruded flaps become pediculated, and shortly afterward, through breakage of the pedicle, a pale body is separated from the original blood-corpuscle. Sometimes the protoplasmic body itself is becoming constricted on different parts of its bulk, and such constrictions may terminate in a separation of smaller lumps from the original body. On some of these lumps, even the net-like structure of the protoplasm is still visible. Thus a larger blood-corpuscle may be divided into smaller lumps of different shapes.

After from one to two hours' observation, the majority of the blood-corpuscles, in part considerably decreased in size through repeated divisions, swell up and are provided with large vacuoles and large, structureless flaps. In this condition the net-work in the protoplasm is evidently broken apart, inasmuch as the granules are no longer connected with each other, but float in the interior of the protoplasm in a sort of motion, for which the term "molecular motion" has been adopted. Lastly, such a swelled protoplasmic body bursts, and the granules are spread in the surrounding fluid, and with this complete death of the blood-corpuscle has ensued. Blood-corpuscles of perfectly fresh oysters die after having been kept for about two hours under the microscope, whereas those from oysters which have been kept out of the sea for a couple of days die much sooner and more rapidly.

The Structure and Growth of Some Forms of Mildew. By William Hassloch, M. D., of New York.*

During researches in which I stained the corneas of dogs and cats with chloride of gold, many of my preparations became mouldy, and, as repeated application of the chloride produced well-marked characteristic violet coloration of the mildew, I succeeded in studying its intimate structure.

The application of one-half per cent. solution of chloride of gold, for from one to six hours, sufficed to stain the parasitic growth from a light-red violet to a dark blue. The preparations were mounted in the common way, in a mixture of distilled water with glycerine, and remained unchanged for months.

With a magnifying power of 500, thallus-threads (mycelia), hyphæ, and conidia could be seen, as well as numerous branching chains of conidia, all united with mycelia. These formations appear finely granular. Many of the granules are not round, but look jagged and pointed; moreover, both the hyphæ and mycelia-threads show, on their periphery, accumulations of minute, generally dark violet, partly pediculated granules, to such an extent as to conceal, in some places, the contours of the plant. For greater amplification I used an immersion-lens of Tolles, with a power of 1200 diameters, and immersion-lenses of Vérick. With these the mycelia, mostly uncham-

* *New York Medical Journal*, November, 1878.

bered, show thin, dark-violet edges, and contain a large number of granules of different sizes, which, almost without exception, are united by fine, violet threads. This arrangement produces an exceedingly delicate, violet net-work in the interior of the mycelium-thread, the meshes of which are either uncolored or only slightly violet. The smallest granules are homogeneous, while the larger ones sometimes contain central spaces, vacuoles, which appear in the optical section as small rings. Occasionally larger vacuoles are seen within the mycelium, each surrounded by a wreath of violet granules. Not only are the majority of the granules connected with each other, but threads pass also from the wall of the mycelium to neighboring granules. Where hyphæ grow from the mycelium, the wall of the latter looks as if perforated, but its outer contour is continuous with that of the hyphæ.

The hyphæ, always of less diameter than the mycelia, are more finely granulated; but there is no doubt that their granules are also connected by exceedingly delicate threads, both among each other and the wall. The majority of the hyphæ are covered with fine granules, occasionally accumulating in groups, either attached with a broad base or by means of a minute stem. Sometimes such a little body, or such groups, may be seen connected by fine threads with granules in the interior of the hyphæ. Just as in the mycelium, we find also in the hyphæ a number of round or oval vacuoles, which, uncolored themselves, are surrounded by a violet outline, or by a wreath of granules.

Many hyphæ terminate in spherical or oblong conidia. Often a second conidium is directly attached to the terminal one, or by means of an intervening hypha. From this may proceed again a hypha, ending in a conidium, and so on, frequently repeated.

The conidia are of two kinds—viz., thin-walled, the walls of which do not surpass those of the hyphæ; or thick-walled, with a relatively broad shell, interrupted only at the union with the hyphæ or an attached conidium. When two or more conidia are near together, that next to the hypha has usually thin walls, while the succeeding ones have markedly thicker walls. Both kinds contain granules, which, without exception, are connected among each other and the conidium-wall, here and there being provided with vacuoles. The smaller of the vacuoles are ungranulated, while the larger contain either single granules or groups of granules, with filamentous connections in all directions. When two conidia are directly attached to each other, the place of union is broad enough to allow of a direct connection of the granules of both conidia.

The thin-walled conidia possess lateral or polar shoots, in the form of sessile or pediculated granules, or of projections of varying lengths, covered with fine granules. The structure of these projections is either homogeneous or reticular. In thick-walled conidia I have never met with such shoots; here the homogeneous, shining shell is always smooth on the outside.

Many hyphæ terminate in simple or compound conidia-chains. These arise with the formation of successive notches, with increasing diameter of the hypha. Such chains are mainly formed by thin-walled conidia, with numerous, either granular or prolonged, buds. These buds not seldom appear dark violet on their ends, while the stem near the conidia is uncolored. There is either an interruption in the wall of the conidium, or a direct connection of the stem of the bud with granules in the interior. (See Fig. 10.)

To obviate the suspicion that these appearances were produced, at least in part, artificially, fresh mould was examined in an indifferent medium, such as bichromate of potash, and a complete correspondence with what chloride of gold showed was found, although in a less marked degree; so that I would

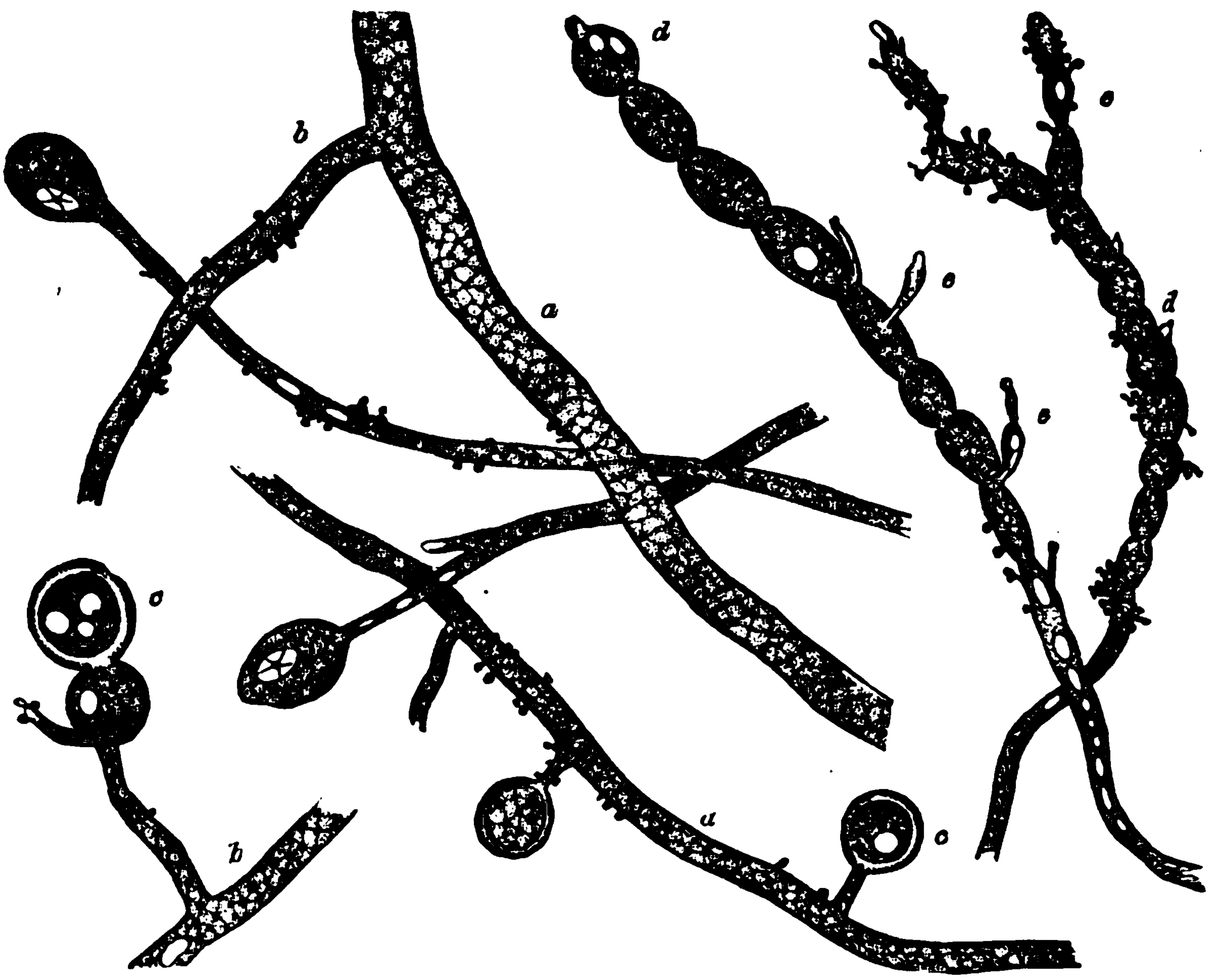

FIG. 10.—MILDEW STAINED WITH ONE-HALF PER CENT. SOLUTION OF CHLORIDE OF GOLD.

a a, threads of mycelium; *b b*, hyphæ; *c c*, conidia; *d d*, chains of conidia. Granular buds are visible on all hyphæ and chains of conidia, while buds are missing altogether on thick-walled conidia, *c c*. At *e e* conical buds or projections are present, the thicker ends of which are compact and stained dark violet, while their stems appear light. Magnified 1200 diameters.

assert that only those who have studied the chloride of gold preparation previously will find the fine threads connecting the granules in a fresh preparation.

I have also examined several kinds of oidium, of which the close relationship among each other, as well as with the spores of mildew, has been repeatedly demonstrated by other observers.

The structure of *beer-yeast* is identical, both in the fresh condition and after staining with chloride of gold, only in the latter case the appearances are more marked than in the former. In fresh preparations, free granules of various sizes are recognized, of which some are at the limit of the visible, even with an amplification of 1200, and groups composed of numerous homogeneous, yellowish, shining, apparently structureless granules, which are connected with each other by extremely delicate threads. The latter are not yellow, but gray. Some granules have fine offshoots, the con-

necting bridges being no longer visible, even with the greatest magnifying powers.

The essential oidia of yeast are, as is well known, mainly oblong bodies, the majority of which contain a large central vacuole. High amplification shows that the outer shell represents a usually homogeneous shining, yellow ring, thickened at *one* pole of the oidium. Within the shell, granules are present, each of which is separated from the other contents by a light seam, and connected with the shell by minute threads. The surface toward the vacuole is either smooth or covered by granules, a part of which projects into the vacuole. The thickened portion of the shell is not seldom perforated by smaller vacuoles, each surrounded by a layer of the yellowish, shining substance. In the interior of the vacuole, isolated minute granules may be found in active motion, while smaller vacuoles contain a varying number of granules, connected among each other and with the shell by finest filaments. (See Fig. 11.)

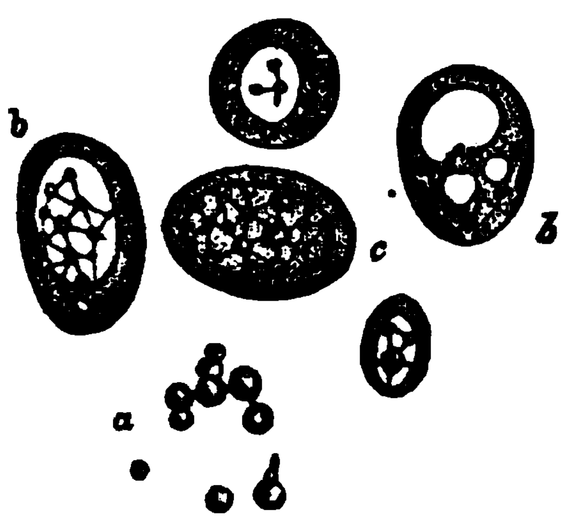

FIG. 11.—OIDIUM OF YEAST.

a, homogeneous granules, partly isolated, partly in shape of chains; *b*, oidia with large vacuoles, whose walls are either compact or granular, or traversed by minute vacuoles; *c*, oidium devoid of a vacuole, its living matter in net-like arrangement, the points of intersection being the granules. Magnified 1200 diameters.

Oidia without vacuoles have always a relatively thin shell, and contain a number of granules of different sizes, which, without exception, are united. Only the yellowish, shining substance of the shell and the granules become dark violet from the solution of chloride of gold; all other parts remain uncolored, or, at most, become only pale violet.

In *fermenting wine*, I met with a great number of small, free granules, with short, rod-like formations (bacteria), and the round or oblong oidia. Numerous oidia form chains of two or more members, the single links of which are united by short, broad bridges. Occasionally a small bud is attached directly, with a broad basis, to a larger oidium. High magnifying power shows that here vacuoles are less numerous, and of markedly smaller size, than in beer-yeast. Each oidium is bounded by a yellowish, shining shell, perforated only at the union with its neighboring oidia, and containing in its interior a varying number of granules of different sizes, all connected by delicate threads. The granules show the same refraction and color as the shell, while the threads between the single granules and the different oidia are colored gray. Smaller buds and smaller isolated oidia are almost always compact, yellowish, shining, and apparently without structure. (See Fig. 12.)

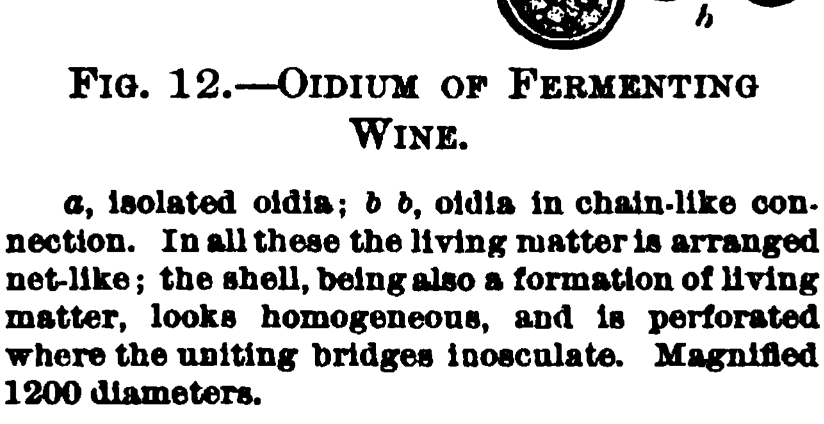

FIG. 12.—OIDIUM OF FERMENTING WINE.

a, isolated oidia; *b b*, oidia in chain-like connection. In all these the living matter is arranged net-like; the shell, being also a formation of living matter, looks homogeneous, and is perforated where the uniting bridges inosculate. Magnified 1200 diameters.

The grayish-white patches occurring in the mouths of infants, known as *thrush*, contain beside epithelia the following: Very delicate granules in active, dancing motion — micrococci; short, single or double oscillating rods — bactaria; delicate threads, straight or variously curved, smooth or granular, and in the latter case occurring in chains, mostly without movement — leptothrix; and finally oidia. After being kept for forty-eight hours in a moist chamber, the mass removed from the mouth shows a number of delicate mycelia, the hyphæ of which have small sporangia. This vegetation is perfectly identical with that of mildew. The oidia correspond in their size to those of wine; many contain large vacuoles, in all details like those obtained from beer and wine, only the color of the shell and the granules is more gray and very slightly yellowish. In preparations kept for forty-eight hours in a moist chamber, many oidia are united in chains, and many show prolongations, the extreme ends of which are always compact and structureless.* (See Fig. 13.)

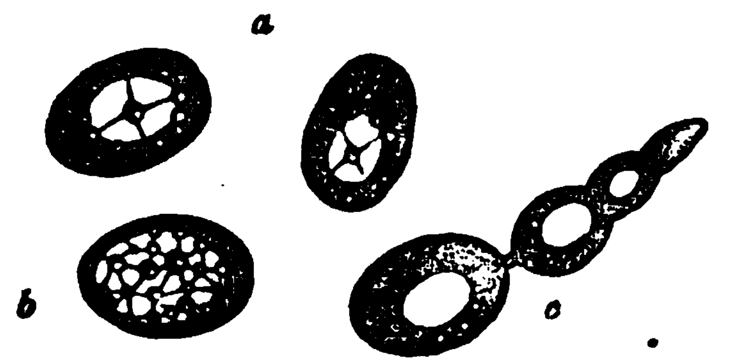

FIG. 13.—OIDIUM OF THRUSH FROM A CHILD'S MOUTH, AFTER BEING KEPT FOR FORTY-EIGHT HOURS IN THE MOIST CHAMBER.

a, oidia with vacuoles, with formation of granules in the latter; within the vacuole single granules, with thread-like connections to the wall; *b*, oidium, with net-like arrangement of the living matter; *c*, chain of oidia in budding; the bud is compact, homogeneous; behind this are links with successively larger vacuoles. Magnified 1200 diameters.

Finally, I have seen in the oidia of acid urine, kept quiet for several days, a structure perfectly identical with that of the mentioned various oidia.

From the description of different forms of the mildew, it is clear that its intimate structure is perfectly analogous to that of animal protoplasm, as it was first described by C. Heitzmann. This investigator, from his observations of the phenomena of motion and growth of animal protoplasm, has arrived at the conclusion that there are two kinds of constituent substances in it,—viz., first, a gray or yellowish substance, which forms the limiting layer or shell of the protoplasmic body, the granules, the central nucleus, and all the connecting threads — the living matter; and, secondly, a liquid not possessed of life, which fills the vacuoles and the meshes between the net-work of the living matter — the protoplasmic liquid.

Only the living matter becomes easily and distinctly violet when the preparation is stained with a solution of chloride of gold.

The net-like structure is plainly marked in the low vegetable organisms

* The fungus of the thrush recently has been studied also by Paul Grawitz ("Zur Botanik des Soors und der Dermatomykosen," *D. Zeitschr. f. prakt. Medicin*, 1877). He made experiments of raising, in transparent, nourishing fluids, and found in fluids rich with sugar, after twenty-four hours, instead of single round or oblong conidia, clusters of oidia in budding process. The more sugar was present in the nourishing fluid, the denser and less transparent were the colonies of the oidia, while in fluids containing less sugar the dumb-bell shapes of the oidia were prevalent. In the latter fluid there occurred chains of oidia, on the uniting bridges of which numerous grape-like buds were visible. In fluids with a small quantity of sugar and salt, pediculated buds grew in several directions from the periphery of oblong oidia, and in one main direction links sprang from the mother body, lastly forming a chain-like thread. The oidia of the thrush, as raised in a fluid rich with sugar, produced, if transported into a dilute fluid, thin mycelia of the same shape in which we see them in fresh thrush. Grawitz holds that the fungus of the thrush is in no relation to the oidium of milk, but rather identical with the mycoderma vini, first described by Cienkowski.

described. Here, too, the yellowish, shining substance, gray in thin layers, which is easily stained violet with chloride of gold, forms a wall or shell of varying thickness, the granules and connecting threads; while the vacuoles and meshes are filled with a liquid which not seldom contains isolated granules.

C. Heitzmann declares that living matter presents at first a compact, homogeneous little lump; that this matter, on growing, is differentiated by the formation of vacuoles into a frame-work, which includes the liquid, not endowed with life; that, finally, at a certain degree of growth, the differentiation of a net-work takes place, the meshes of which contain the not living fluid. These stages are demonstrable also in growing mildew and oidia. The first visible form-elements are homogeneous granules, and the first appearing buds are compact little projections, either globular or prolonged. The first differentiation consists in the occurrence of a central vacuole, and only after a certain development has been attained does the protoplasm appear in the form of a net-work.

That the yellowish or gray substance is in fact the living matter, is proved by the formation of buds on the hyphæ, conidia, and oidia, and the conidia-chains. The minutest buds are, in every instance, direct prolongations of the shell, or a granule contained in the interior.

IV.

THE PHASES OF DEVELOPMENT OF LIVING MATTER.*

THIS article is a translation of a publication in German in 1873. What at that time were considered to be phases of life of the protoplasm, must to-day be taken as different phases in the development of living matter, one of which is its reticular arrangement in protoplasm. This latter term, then, in the present view, is applicable to only *one* of the phases of development.

Amœbæ. In specimens taken from an infusion on the third or fourth day after its preparation, we meet with a few lumps of protoplasm, not over 0.008 mm. in size, in slow locomotion. These lumps are shining, yellowish, and formed by a very dense reticulum of living matter; some of them contain vacuoles. A nucleus is not recognizable in such a youthful amœba. A few days later on, besides amœbæ of the described size, others are found which are larger, finely granular, and execute lively changes of shape and locomotion. Every one of these amœbæ has a pale gray, homogeneous nucleus.

Specimens taken from the infusion in the third or fourth week contain, in addition to younger forms, many amœbæ, with a varying number of coarse, shining, yellowish granules. These are

* Untersuchungen über das Protoplasma. III. Die Lebensphasen des Protoplasmas. Sitzungsber. der Akademie der Wissensch. in Wien. June, 1873.

either scattered through the body of the amœba, or accumulated in groups, but little exceeding in size that of the nucleus. Both kinds of granules are connected, by means of delicate filaments, with the reticulum of the living matter of the lump. The pale gray nuclei of such older amœbæ always exhibit vacuoles.

If we add a drop of glycerine, diluted with one-half water, to a specimen containing amœbæ of early formation, each amœba will, the moment it is reached by the glycerine, suddenly contract into a homogeneous, yellowish, very shining lump, the size of which is only a small fraction of its former circumference, or the amœba shrivels to a scolloped lump, which by the bursting of peripheral vacuoles becomes in a few seconds nearly homogeneous. Such lumps remain, as a rule, unchanged.

Amœbæ of a later period do not react uniformly to glycerine. If both a finely and coarsely granular amœba should be present in the field of vision, the latter, on addition of glycerine, will rapidly be transformed into a homogeneous lump, while the former will slowly shrivel, sometimes only become corrugated on its surface, and retain its finely granular character, becoming, however, motionless and globular. Most of the lumps, sprung from coarsely granular amœbæ, enter the globular condition slowly. Some even remain unchanged. Whether this difference is due to difference of concentration of the glycerine which reaches different amœbæ, even in one field of vision, I am unable to decide.

By draining off the glycerine and replacing it with water, all lumps are gradually transformed into globules, but none of them recover mobility.

The series of changes which the coarse granules of the blood-corpuscles of *craw-fish* undergo, without the addition of any reagent, are described in Chapter II., page 23. An originally solid, homogeneous lump of living matter, in a short time, under our very eyes, becomes at first vacuoled, and at length transformed into a delicate reticulum.

Cartilage-corpuscles. In comparing the corpuscles of cartilage of mammals (I have examined the cartilage of the knee-joints of dogs, cats, and rabbits) of different age, marked differences are observed, dependent on the age of the animal.

The cartilage cavities of a pup, five days old, hold protoplasmic bodies, the nuclei of which are homogeneous, yellowish, and very shining, and sometimes contain vacuoles. Besides, there are numerous smaller cavities entirely filled with a mass,

in every particular like the nuclei of the cartilage-corpuscles mentioned before. (See Fig. 14.)

When the solid substance forms the nucleus of a protoplasmic body, conical spokes arise from its periphery, which blend with the reticulum of the protoplasm. When the solid substance alone fills the cavity, the spokes traverse the light rim between its periphery and the border of the basis-substance of the cartilage.

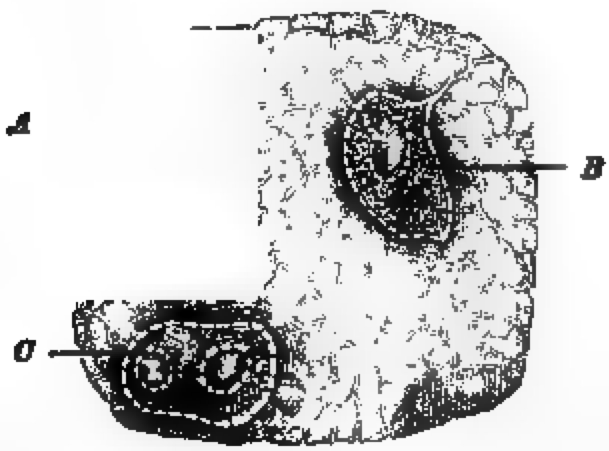

FIG. 14.—CARTILAGE-CORPUSCLES FROM A FRONTAL SECTION OF THE CONDYLE OF THE FEMUR OF A PUP, FIVE DAYS OLD.

A, solid vacuoled corpuscle; *B*, corpuscle with one solid nucleus; *C*, corpuscle with two solid nuclei. Magnified 800 diameters.

In the cartilage of a pup, six weeks old, cavities are found which contain granular protoplasm, and lumps of a homogeneous, yellowish, shining substance, variously distributed. (See Fig. 15.) There are some cartilage-corpuscles with a central solid mass of the shining substance; other corpuscles with several solid lumps of different size; lastly, corpuscles in which the shining substance appears as an incomplete shell, in the optical diameter as a semi-lunar ledge. Cavities filled with the

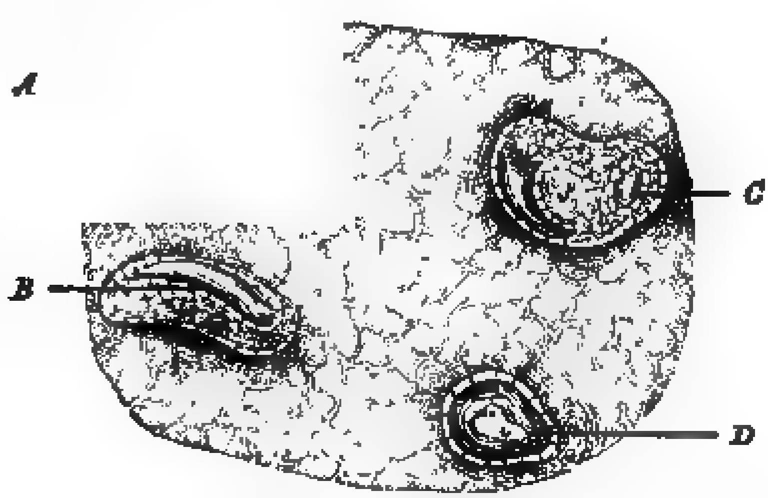

FIG. 15.—CARTILAGE-CORPUSCLES FROM A SAGITTAL SECTION OF THE CONDYLE OF THE FEMUR OF A PUP, SIX WEEKS OLD.

A, corpuscle holding, besides the nucleus, several larger granules, *B*, corpuscle with a solid oblong nucleus at the periphery, *C*, corpuscle with two solid nuclei; *D*, solid, vacuoled corpuscle. Magnified 800 diameters.

shining substance are less frequent than in the cartilage of a newly born animal, and the substance often exhibits larger vacuoles.

In the thin layer of cartilage of a dog, eight to ten years old, the compact shining substance is relatively scarce, and, as a rule, traversed by vacuoles. Most of the cartilage-cavities contain a pale granular protoplasm and vesicular nuclei with dark contours, and a varying number of nucleoli. (See Fig. 16.)

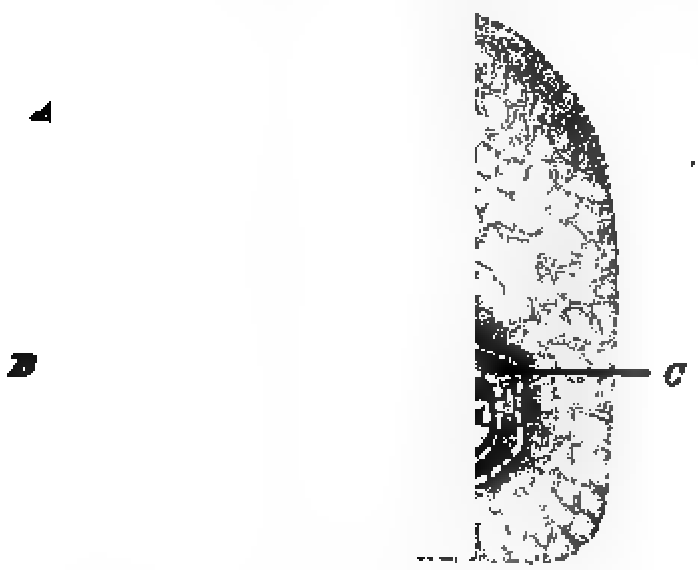

FIG. 16.—CARTILAGE-CORPUSCLES FROM A SAGITTAL SECTION OF THE CONDYLE OF THE FEMUR OF A DOG, EIGHT TO TEN YEARS OLD.

A, corpuscle with several gray lumps besides the vesicular nucleus; *B*, corpuscle with an hour-glass-shaped nucleus; *C*, corpuscle with an oblong central nucleus. Magnified 800 diameters.

These features were found in the middle region, between the articular surface and the border of the epiphyseal bone. In young animals, the yellow substance, on an average, occurs the more the nearer to the bone the examination is made. Immediately on the border of the bone the centers of the large cartilage-cavities, which are inclosed by a calcified basis-substance, are occupied by large masses of the yellow substance, which in this situation is supplied with numerous vacuoles, and with lower powers appears coarsely granular. Each central lump is surrounded by a zone of a pale, finely granular or structureless substance, which is separated by a light, narrow rim from the

FIG. 17.—BONE-CORPUSCLES FROM A LONGITUDINAL SECTION OF THE THIGH-BONE OF A PUP, FIVE DAYS OLD.

P, corpuscle with a vacuoled shining nucleus; *B*, basis-substance. Magnified 800 diameters.

calcareous basis-substance. Such formations are absent in old animals.

Bone-corpuscles. In comparing bone-corpuscles of a newly born with those of an old dog, a difference in the structure is apparent. The cavities of the former contain a central globular, oblong, or angular vacuoled lump of a yellowish color, and intensely shining. Around this lump there is a pale, finely granular protoplasm; the spokes springing from the central lump blend with the pale protoplasm, or, in places where the latter is apparently wanting, with the basis-substance of the bone. We not infrequently meet with bone-cavities entirely filled with the yellow, shining substance. (See Fig. 17.)

In the bone of a dog, about ten years old, there are but few corpuscles, with pale yellow shining nuclei; whereas cavities with pale protoplasmic bodies and pale nuclei largely prevail.

Fig. 18.—Bone-corpuscles from a Longitudinal Section of the Thigh-bone of a Dog, Eight to Ten Years Old.

P, corpuscle, with a vesicular nucleus; *B*, basis-substance. Magnified 800 diameters.

The latter represent gray, vacuoled lumps or vesicles, with one to two yellow shining, or one to three gray opaque nuclei, of which the former usually are larger than the latter. (See Fig. 18.)

Corpuscles of the Medulla of Bone. The medulla of bone also exhibits marked differences of age. In the medullary spaces of a shaft-bone of a new-born pup, the apparently homogeneous basis-substance holds small, yellowish, shining lumps, either globular or elongated, either homogeneous or vacuoled. Besides, there are pale protoplasmic bodies with globular nuclei, similar in aspect to the lumps just described; also pale bodies are seen without nuclei, but in their place cavities with one or two opaque

corpuscles; and, lastly, we meet with pale, finely granular protoplasmic bodies devoid of nuclei and nucleoli.

As the growth of the animal advances, no medullary spaces are found in the bone, but canals for vessels instead. The medullary elements in the space between the wall of the blood-vessel and the border of the bone are mostly spindle-shaped, and either yellowish, vacuoled lumps, or pale protoplasmic bodies, with and without distinct nuclei and nucleoli. In all instances the compact lumps, the pale protoplasmic bodies, the nuclei and nucleoli, are bordered by light rims, which are traversed by radiating spokes.

In old animals, protoplasmic bodies of the above description are rare; in the marrow spaces of the shaft-bones they are usually transformed into fat.

My conclusion, drawn from these observations, is that the *protoplasma shows differences according to its age.*

The shape of the youngest protoplasm is that of a compact lump of the living matter, with the following properties: It is homogeneous, has a yellow tint of varying intensity and shade, a considerable luster, and admits of being stained red by a solution of carmine, and violet by a solution of chloride of gold.

In this condition, with our present means of examination, no reticulum is demonstrable. This condition is similar to that of a tetanic lump of a contracted amœba, and identical with the condition of the living matter which I termed, in 1872, "hæmatoblastic," in which the living matter produces both red blood-corpuscles and the wall of the blood-vessel. For small lumps of this substance, which are directly converted into red blood-corpuscles, the term "hæmatoblastic" remains applicable, though the hæmatoblastic substance has a significance wider in sense than it seemed to have at the time the name originated.

The first noticeable differentiation in young protoplasm consists in an accumulation of liquid in vacuoles. The vacuoled condition of hæmatoblastic substance is the first step in development, as observed in the lumps and nuclei of the tissues of somewhat older animals. The first formation of the walls of a vessel depends on this differentiation, inasmuch as the vacuole represents the earliest cavity of a vessel.

Owing to an accumulation of a liquid in several closed cavities of the young protoplasm, the living matter assumes the shape of a frame-work. The points of intersection of the frame becoming granules by a rupture of many of the walls of the vac-

uoles, a net-work is established, which represents a later phase of development of protoplasm. The more coarse, yellow, and shining, and the more densely arranged the points of intersection of the living reticulum are, the nearer it is to its youth; on the contrary, the more delicate, devoid of color and luster, the granules are, the more advanced is the age of the protoplasm. That under certain circumstances the living matter in the protoplasmic lump, by endogenous formation, reproduces its own kind, is proved by observations of older amœbæ. Here the coarse granules are newly formed living matter in a juvenile condition.

With this explanation we can easily understand the differences of age in the elements of tissues, described above. The originally homogeneous lump of protoplasm, with increase of size, is transformed in its peripheral portion into a net-work, whereas the central portion, the nucleus, remains homogeneous. Next a differentiation into a frame-work, and in turn into a net-work, takes place in the central lump, the nucleus, so as to leave smaller, compact centers, the nucleoli. This condition furnished the scheme of the "cell" of the authors.

At last the differentiation into a net-work has involved the whole protoplasmic body. At this stage no nucleus, and later on even no nucleolus, is perceptible, for the whole body is split up into a reticulum, with coarser and finer points of intersection, and this condition immediately precedes the formation of a basis-substance.

The living matter passes through these stages, not only in the normal, progressive development of all tissues, but, as I will demonstrate later, also in the process of inflammation, though here in a reversed manner.

The first assertions as to a difference of the nuclei depending on age are made by Th. Schwann.* According to this author, the nuclei in the juvenile condition are solid, later become hollowed, and at length completely disappear, or are absorbed. S. Stricker † maintains that the nucleus of the first globule of segmentation originates in the protoplasm, and that the nucleus in its youth represents a lump, while with advancing age it may be transformed into a vesicle.

* Mikroskop. Untersuchungen über die Uebereinstimmung in der Structur und dem Wachsthum der Thiere und Pflanzen. 1839. Pages 205 and 211.

† Handbuch der Lehre von den Geweben. Art. "Allgemeines über die Zelle." 1868. Page 24.

Lastly, I would take into consideration a peculiarity in the phases of life of the protoplasm, as evidenced by observations on living corpuscles in a healthy as well as a diseased condition.

Young, compact protoplasm is in a high degree possessed of the property of coalescing with analogous protoplasm, and thus change its configuration, whereas it exhibits the property of active mobility in a slight degree only. The power of locomotion is entirely absent. Under certain circumstances—f. i., on the border of ossification of the epiphyseal and intermediate cartilage—the living matter is split into pieces, broken apart. The best representation of a normal division I have observed in the hæmatoblastic substance within the cavities of the cartilage, the results of which division are the hæmatoblasts.

The power of active motion evidently increases by degrees; the more the liquid accumulates in the mesh-spaces of the protoplasm, within certain limits of its bulk, the smaller and paler, therefore, the granules become. The "pale and finely granular" protoplasm of the authors, which holds a very delicate reticulum, has also the most marked capacity of locomotion, upon raising its temperature to that of the whole body in a normal condition and in fever. The capacity of compact nuclei and nucleoli of changing shape and place, on the contrary, seems to be very limited or wanting. We must consider the protoplasma of the latter formations as relatively the younger, so far as its shape is concerned.

The Cell-theory in the Light of these Researches. The theory of the animal cells, as established by Th. Schwann,* was greatly altered in 1861, by the researches of Max Schultze.† Since then, the best observers have agreed that "cell" was to designate a lump of protoplasm, without a membrane and even without a nucleus. It was added that the protoplasm appeared structureless. E. Brücke's‡ attempt to show that the lump was an "elementary organism" was, for that time, in a certain sense, progress.

The term "cell" remained, although a different meaning was attached to it than at the time of its origin, and all observers

* Mikroskopische Untersuchungen über die Uebereinstimmung in der Structur und dem Wachsthum der Thiere und Planzen. Berlin, 1839.

† Ueber Muskelkörperchen und das, was man eine Zelle zu nennen habe. Müller's Archiv. 1861.

‡ Die Elementarorganismen. Sitzungsber. d. Wiener Akademie der Wissensch. 1861.

seemed to consider it a necessity to include all possible form-elements within this improved scheme of a cell.

S. Stricker,* in 1868, for instance, discusses the question how large a lump of protoplasm ought to be to entitle it to the name of a cell, and comes to the conclusion that we should speak of a cell only if the lump exhibits growth and reproduction. At that time it was already known that, with the highest powers of the microscope, very minute, just perceptible, granules grow under our very eyes. The doctrine of the so-called zymotic diseases almost necessitates the assumption that the carriers of the contagion are organisms, not subject to our observation even with the best lenses. Are not the innumerable corpuscles in decomposing liquids individual organisms in spite of their minute size, which renders them hardly perceptible even with our best optical apparatus? And all these minute organisms should be called cells. Very probably, a granule of living matter may be altogether too small to be perceived, and such a granule will agree as little with the idea of a cell as it will with the idea of an elementary organism.

What at that time was called a structureless, elementary organism, a "cell," I have demonstrated to consist only in part of living matter, while even the minutest granules of this matter are endowed with manifestations of life. The cell of the authors, therefore, is not an elementary, but a rather complicated organism, of which small detached portions will exhibit amœboid motions.

The nucleus cannot be considered an essential part of the cell, for all good observers know that there are cells destitute of nuclei, and some authors have distinguished nucleated cells from "cytodes"—cell-like bodies devoid of nuclei. (See page 2.)

We can escape from the difficulties of a definition only by abandoning the designation "cell," in the sense of the zoölogists. By this, our usual terminology will remain unaltered. The amœba, f. i., or the colorless blood-corpuscle, the protoplasmic lump in the colostrum, the pus-corpuscle, are formations to which the term "cell" is not usually applied. We need no such word for properly designating what we mean by saying the amœba, the colorless blood-corpuscle, etc., are alive; or the amœba, the colorless blood-corpuscle, are organisms.

Such were my conclusions in 1873 *(l. c.)*, and here I wish to add a few remarks more as to the propriety of the term "cell."

* Handbuch der Lehre von den Geweben. Art. "Allgemeines über die Zelle." 1868.

The size of a living body is not included in the definition of an organized individual. In the infusion, f. i., we see growing granules, just perceptible to the highest magnifying powers of the microscope, in a fluid in which none were seen a short time before. The smallest individuals which we are capable of seeing with the best microscopes of to-day, are granules; but we must admit that germs or particles of living matter may be present in the air or in fluids in infinite numbers, which cannot be seen at all, and become visible only after having attained a certain size. How complicated the structure of a minute particle of living matter may be, we can hardly imagine; what we do know is, that the so-called "cell" is composed of innumerable particles of living matter, every one of which is endowed with properties formerly attributed to the cell-organism.

The observation of the phases of development of the living matter demonstrates that the term "cell" was attached to only a limited number of forms, during the changes that take place in a growing granule of a substance known to be the seat of life. As the term "protoplasm" was adapted to the original idea of the cell, it also meant only one or a few phases in the development of a lump of living matter. (See Fig. 19.)

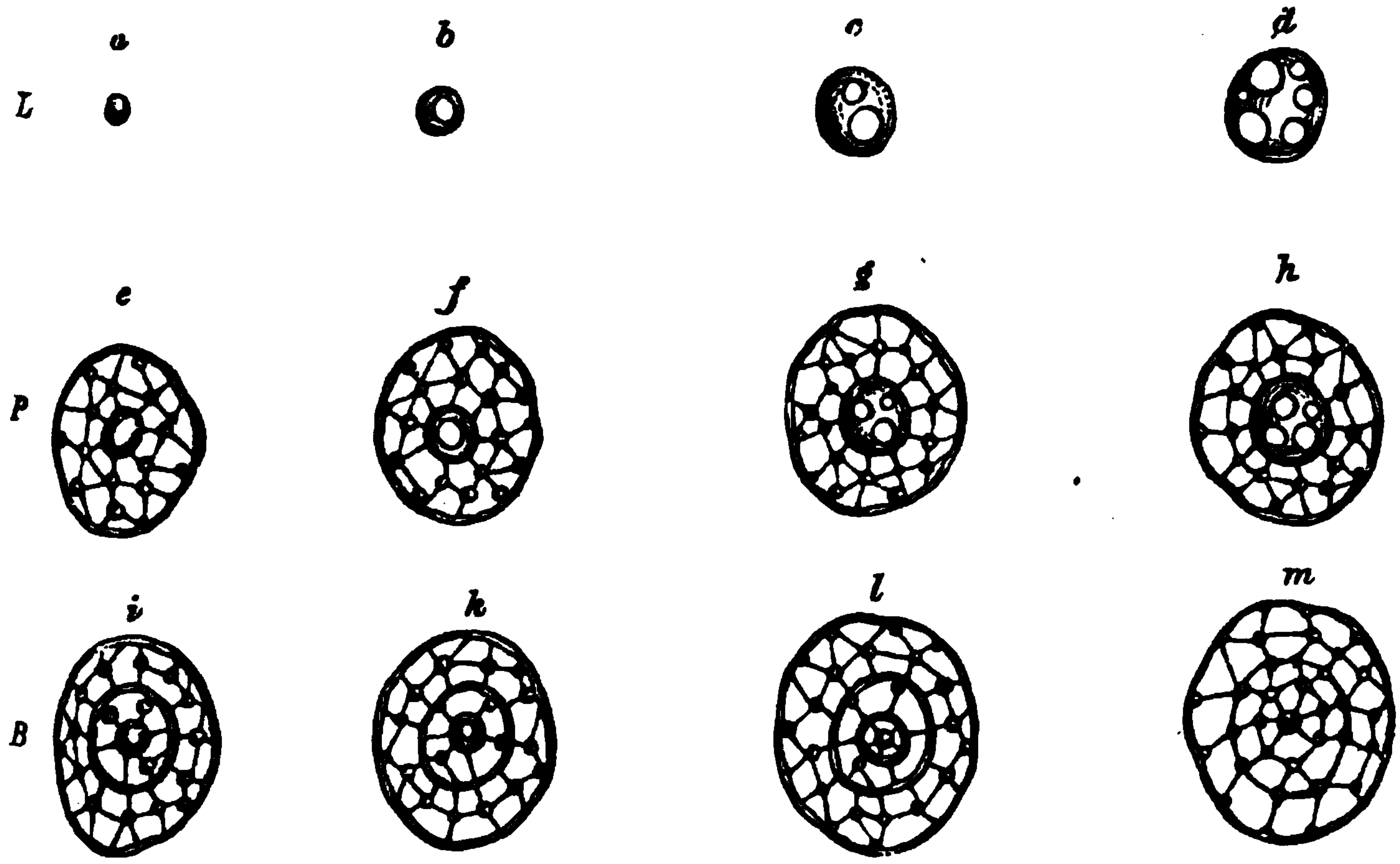

FIG. 19.—DIAGRAM OF THE PHASES OF DEVELOPMENT OF THE LIVING MATTER.

L, series of development of a small granule, *a*, into a vacuoled lump, *b* and *c*, and into a frame-work, *d*. *P*, series of development into protoplasm of a reticular structure; the so-called "cell," *e*, with a solid, *f*, *g*, *h*, with vacuoled nuclei. *B*, series of development tending toward the formation of basis-substance; in *i*, the nucleus reticular, the nucleolus solid; in *k* and *l*, the nucleolus splitting; and in *m*, the original granule *a* transformed into a finely reticular mass, destitute of nucleus and nucleolus.

The series of progressive changes, tending toward the formation of protoplasm, proves that the original granule is the morphologically simplest appearance for our present means of observation. The growth and splitting of the granule results in the appearance of a reticular lump, a rather complicated organism, hitherto termed "protoplasm"; and thus the relation between the two is about the same as that between an ovum and a grown animal body. That a single lump of protoplasm—f. i., an amœba—is endowed with all fundamental vital properties attributed to the whole organism—f. i., a mammal—is acknowledged to-day by all physiologists. M. Foster attributes to the amœba, which he considers an "undifferentiated protoplasm," the following properties: It is contractile; it is irritable and automatic; it is receptive and assimilative; it is metabolic and secretory; it is respiratory; it is reproductive.

All this holds good for isolated lumps of living matter, suspended in the liquids of the animal body. Is it applicable to complex masses of this matter—to tissues?

As I shall demonstrate later, there is no such thing as an isolated, individual cell in the tissues, as all cells prove to be joined throughout the organism, thus rendering the body *in toto* an individual. What was formerly thought to be a cell is, in the present view, a node of a reticulum traversing the tissue. Neither is there a good reason for speaking of protoplasm, or for claiming that it is protoplasm which builds up the animal body; for living matter appears in the organism in various shapes, and it is but one of these, viz., an advanced stage of development of the living matter, which was hitherto termed "protoplasm."

According to my observations, we have not to deal with cells as form-elements, either in the fluids or in the tissues of the animal body, but only with living matter, varying in its appearance from the just perceptible granule to the bulk of the body of the largest animal. Single lumps of living matter may either look homogeneous or show a net-like arrangement, whereas the body of an animal is a continuous mass of living matter or network arrangement, and contains fluids in blood and lymph vessels, in which there are suspended isolated bodies, either homogeneous or reticular in structure, as analogous to the granules which float in the vacuoles of an amœba. The difference in the aspect of the tissues depends on the presence of a lifeless basis-substance only, a derivative of the lifeless "protoplasmic

fluid," while the living matter of the tissues exists mainly in the reticular stage, and is interconnected without interruption throughout the body.

The question arises, are we justified in speaking of "cells" as the formative elements of plants? The living matter of plants is not materially different from that of animals, so far as its appearance is concerned. W. Kuehne discovered vegetable lumps of protoplasm exhibiting amœboid motion and locomotion, almost identical with that of amœbæ. In fresh tissues of plants the living matter was for a long time known to be endowed with motion, as the granules were seen by E. Brücke and others, floating briskly in a liquid. My own limited researches enable me to assert that the granules of living matter in vegetable protoplasm are, as a rule, united in the shape of a reticulum in the same manner as in animal protoplasm. Besides, the researches of W. Hassloch (see page 40) elucidate the identity of both animal and vegetable living matter in a satisfactory manner. I may add that all cells of the vegetable organism are uninterruptedly connected by means of delicate offshoots, piercing the walls of the cellulose. The granules of amylum are transformed living vegetable matter. The plant *in toto* is an individual, and not composed of individual cells.

The present generation of histologists will very probably never realize the harm done by the misnomer "cell," so firmly established during the last forty years. Nevertheless, I shall make an attempt to replace former misnomers by new words and terms, the originator of which is L. Elsberg.* He says:

> The formerly unquestioned "cell" views of histologists are giving way to a more correct appreciation of the living matter of the body. In pathology, as in physiology, the cell doctrine has led to great advances in accurate knowledge as an aid and means of research, but it has outlived its usefulness. Instead of adhering to Virchow's comparison, "that every higher organism is like an organized social community or state, in which the individual citizens are represented by the cells, each having a certain morphological and physiological autonomy, although, on the other hand, interdependent and subject to the laws of the whole," we now compare the body to a machine in which, though there are single parts, these are materially connected together, and no part is at all autonomous, but all combine to make up one individual. According to the former view, the body is composed of colonies of amœbæ; according to the latter, the body is composed of one complex

* Notice of the Bioplasson Doctrine. Transactions of the American Medical Association, 1875. Contributions to the Normal and Pathological Histology of the Cartilages of the Larynx. Archives of Laryngology, 1882.

amœba. I have named this biological doctrine, which is based on Heitzmann's discoveries, the "bioplasson doctrine," using the word "bioplasson" only as a technical synonym for the two words "living matter"; and I use the term "plastid," proposed by Haeckel, or that of "bioplast," proposed by Beale, to denote a so-called "protoplasmic body," or a form-element, a formerly so-called "cell." Perhaps it would be the best to restrict the word "bioplast" to a small mass of living matter exhibiting no differentiation, and to distinguish from it as "plastid" the larger mass showing an interior structure more or less like the fully developed corpuscles. Thus, I would always use the term "plastid" in the place of "cell."

The word "protoplasma" is etymologically incorrect for designating living and formative matter, as it has already been used by some authors with a meaning other than the simple one here intended; and as it has not yet become so common that its retention or rejection is a matter of much consequence, I propose the designation "bioplasson doctrine."

The word plasma (τὸ πλάσμα) really means the *formed*, that which is formed, and plasson (τὸ πλάσσον) the *forming*, that which forms or does the forming. The distinction is the one so justly insisted upon by Beale in his discrimination between *germinal* or *living matter* and *formed material*. The term plasm may, perhaps, be appropriately applied to the material formed from the fluid of living matter, the intermediate or intercellular substance of authors; but the term plasson only can be applied to active, living, forming matter. Proto (πρῶτος) is a prefix signifying first, primary, primordial; and protoplasma has been used by some to denote the original or first-formed organic matter. But the term we are in need of for our biological doctrine is one that shall be an expression for living formative matter in its simple elementary form; and for this purpose, it seems to me, bioplasson may appropriately be chosen.

The General Constitution of the Body, as Recognized by Single Plastids. In 1879* I published facts which, perhaps, are of some value to practical medicine, and certainly elucidate the practical value of the new discoveries. I reprint my assertions with the only alteration that, in accordance with the new terminology, as suggested in the foregoing article, instead of "protoplasm" and "protoplasmic body," I use the terms "bioplasson" and "plastid."

The amount of living matter within a limited bulk of a plastid varies greatly in different individuals. It is obvious that what is called a healthy or vigorous constitution is based upon a large amount of living matter in the body, the new growth of which in morbid processes is very lively; while a strumous or scrofulous or phthisical constitution must be caused by a relatively small amount of living matter, the new growth of which is

* "The Aid which Medical Diagnosis Receives from Recent Discoveries in Microscopy." Archives of Medicine, February, 1879.

ɜanty in morbid processes. In other words, a plastid will exhibit ɔarse granulations, or it will be almost homogeneous-looking nder the microscope, owing to the large amount of living matter n strong individuals of good constitution, while a plastid taken rom a person with weak or strumous constitution will be finely granular, as but little living matter is present in it.

Two years ago, I announced* that pus-corpuscles show remarkable differences in their minute structure in different individuals. Those from otherwise healthy and strong persons are yellow, almost homogeneous, or coarsely granular, I said, while those from broken-down, weakened, or strumous persons are pale gray and finely granular. This fact has been made use of in hundreds of cases, when pus-corpuscles, mainly in urine, were brought by different physicians to my laboratory for examination, for telling whether the pus belongs to a good or a bad constitution, of course without any knowledge of the patients themselves. I was right in every instance; not one mistake has occurred.

About one year ago I announced† that the colorless blood-corpuscles also demonstrate striking differences as to their minute structure, according to the general constitution. I said that the colorless blood-corpuscles are coarsely granular and slow in their amœboid motions under the microscope, if taken from healthy, vigorous, strong persons; on the contrary, they are pale gray, finely granular—viz., poorly provided with living matter—in broken-down or phthisical individuals. I expressed my hopes that at some future time practical use might be made of these differences. To-day my hopes have turned, after three years' earnest study, into accomplished facts.

The method of examination of the blood for our purpose is extremely simple. We oil the edges of a thin covering-glass on one side with a curled piece of paper, serving as a brush. Prick with a pointed pin the palmar surface of the thumb, near the wrist-joint, thus giving a good convex surface, and being least incommoded by the injury. Squeeze out a small drop of blood, the size of which has to be learned by some practice. Place the glass slide on the drop for transportation, and immediately cover up the specimen with the covering-glass, the oiled edges looking toward the slide. Such a specimen holds the blood in a living

* See page 32.

† "On the Nature of Suppurative Processes of the Skin." A paper read before the County Medical Society of New York, 1877. Unprinted.

condition at least one hour. It is not necessary to use the heated stage, because the colorless blood-corpuscles exhibit their structure in an ordinary comfortable temperature of the room—nay, sometimes show slight amœboid motions. The magnifying power should be at least 800 diameters, the lens to be used being best a one-tenth of an inch immersion. As a matter of course, the lens we use must be first-class. Considerable skill is required for such studies, which embrace first the knowledge of the structure of the bioplasson in general. A few months'—nay, a few weeks'—thorough study under the direction of a reliable teacher will suffice to enable every one to see what really can be seen in the plastids, and to entitle him to judge also of the differences. I never had difficulties in demonstrating the net-work structure of the plastids to any one who was in earnest with his microscopical studies, and took them for more than play. After having obtained a certain practice, one is enabled to tell differences in the anatomy of the colorless blood-corpuscles with a power of 500 diameters only.

Several years ago, I was first struck by the fact that the elements establishing the condition of catarrhal pneumonia and of tuberculosis, both acute and chronic, are decidedly pale and finely granular. Next I learned that pus and colorless blood-corpuscles of strong men are partly homogeneous, or at least coarsely granular. Then I followed these studies by examining the blood of different physicians who came to work in my laboratory, and who could give reliable histories of both their families and their own bodies. Thus I have arrived at a point of perfection which allows me to tell the constitution of a person without knowing anything of his former life.

Besides the differences in the structure of the colorless blood-corpuscles, as described above, valuable hints may be obtained from other circumstances. The number of colorless blood-corpuscles in a given drop of blood is surprisingly different in different persons; the better the constitution, the fewer are these bodies. A sleepless night, however, is sufficient to increase their number, which fact often enabled me to tell physicians, by examination of their blood, whether business was going slowly or lively, the latter inducing sleepless nights, or repeated awakening by patients, or so-called nervousness.

Catarrhal processes, so-called colds, of any of the mucous membranes, lead to increase of the number of the colorless blood-corpuscles; a chronic condition of these processes is indicative

of a poor constitution *per se.* The colored blood-corpuscles greatly vary in their yellow tinge in different persons; the paler this tinge is, the more readily we can tell pale looks of the face or chlorosis. The colored blood-corpuscles stick together in coin-like rows only when the plasma holds a larger amount of fibrin; in the blood of persons with a poor constitution, such rows do not occur; in individuals of moderate vigor, the rows temporarily may be missing, at other times present. In the blood of persons of good constitution, who had passed through severe ailments, I several times found both coarsely and finely granular colorless blood-corpuscles, just as in originally healthy persons who, by chronic diseases, become broken down. In fact, the microscope reveals so much of the general health of a person that more can be told by it, in many instances, than by the naked eye, or by physical examination.

Life insurance should be based upon microscopical examination, as well as on percussion and auscultation. Marriages should be allowed, in doubtful cases, only upon the permit of a reliable microscopist. Last season a young physician asked me whether I believed in the marriage among kindred. He fell in love with his cousin, and so did the cousin with him. I examined his blood, and told him that he was a "nervous" man, passing sleepless nights, and had a moderately good constitution. The condition being suspected in the kindred lady, marriage was not advisable for fear that the offspring might degenerate. So great was his faith in my assertions that he gave up the idea of marrying his cousin—offering her the last chance, viz., the examination of her blood. This beautiful girl came to my laboratory, and, very much to my surprise, I found upon examination of her blood a first-class constitution. The next day I told the gentleman, "You had better marry her."

As a matter of course, every particle of the organism, either in a normal or in a morbid condition, will exhibit characteristics as attributed to the colorless blood-corpuscles. The bioplasson is one uninterrupted mass throughout the body, and is connected from the top of the head to the heels, in what we call tissues.

Several months ago, Dr. Paul F. Mundé brought me a specimen of the size of a pea, which, he said, he found in a large amount of fluid blood vomited out half an hour before by a patient. After immediate examination of a section from the specimen, I told the doctor that his patient was a pale, emaciated, narrow-chested person, who had catarrhal pneumonia, which led by localized gangrene to sloughing of the piece of the lung, on which a broken blood-vessel was visible. I foretold, besides, that the patient would die within one year. I explained to the doctor and to Dr. L. Elsberg, who also was present in the laboratory, what led me to such a diagnosis and prognosis. There were visible alveoli of the lung, and both the walls of the alveoli and their calibers were crowded with inflammatory corpuscles, coagulated fibrin being absent. These are symptoms of catarrhal pneumonia. In some parts

clusters of micrococci could be seen—characteristic of putrefaction, therefore gangrene of the tissue. The inflammatory corpuscles looked very pale and finely granular, the evidence of a bad, phthisical constitution, and all these signs together allowed the diagnosis of a limited viability, hence the disastrous prognosis. The doctor told us that no physical symptoms could be found in the lungs justifying my diagnosis. Still he admitted right away that the patient was a pale-looking, thin, and narrow-chested young man, whose brother had been sent to Florida some time ago for chronic tuberculosis of the lungs. One week afterward, the doctor came to tell me that the physical symptoms at present were so marked in the lungs, that the diagnosis of catarrhal pneumonia was evident. Seven weeks afterward the patient was dead.

The facts here laid before the medical profession may convince even the most skeptical physician that microscopy is destined to play an important part in the science of medicine. Let us proceed in skillful, honest work, and we shall succeed in raising the standard of microscopy still higher, and make it not only a valuable, but rather an indispensable, assistance to clinical work. Much more could and should be done in this country by the profession at large than is done at present, for the perfection of that most interesting and useful science, the science of ourselves—Biology.

Only little is to be added to these assertions. Several years' more study has convinced me of their correctness, and the difference in the appearance of bioplasson, according to the difference in the general constitution, is so striking as to admit of a diagrammatic representation, for which we may choose pus-corpuscles. (See Fig. 20.)

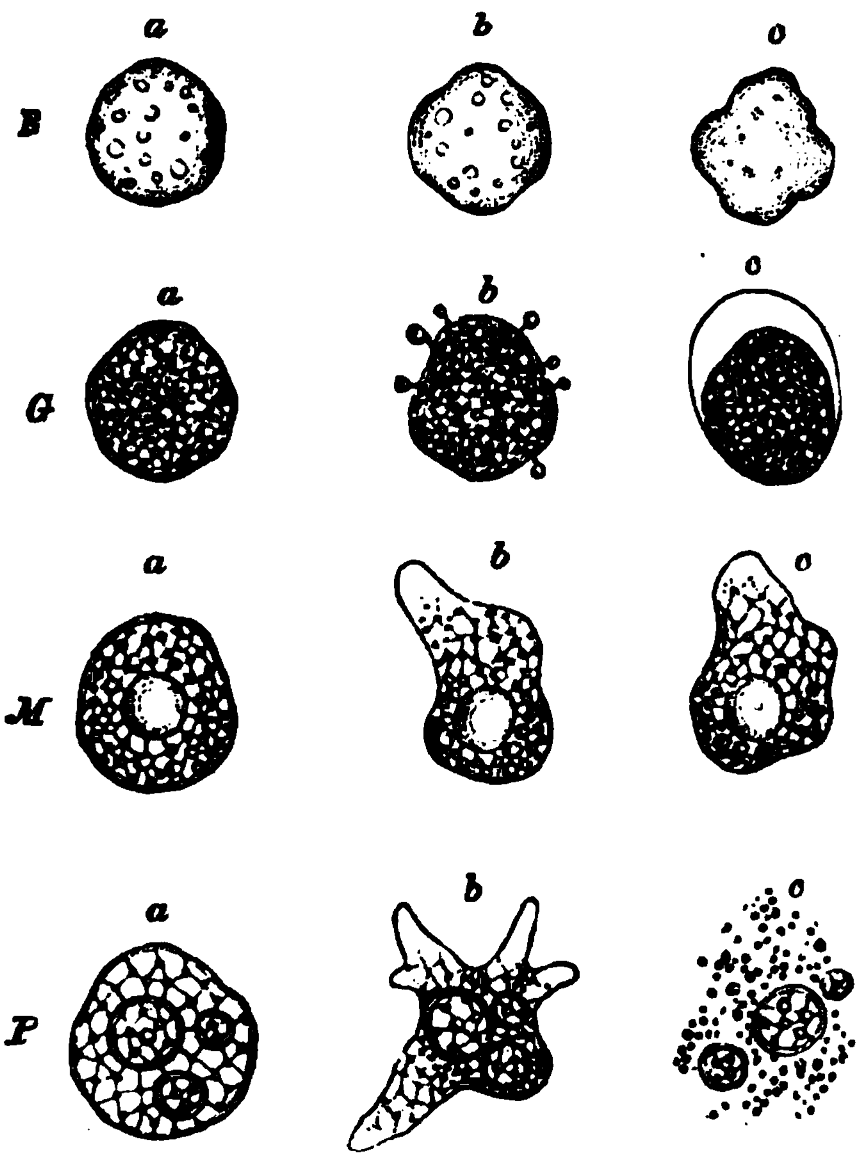

FIG. 20.—DIAGRAM OF PUS-CORPUSCLES OF PERSONS OF A DIFFERENT CONSTITUTION.

E, pus-corpuscle of an excellent constitution; the bioplasson nearly compact, containing a few small vacuoles, alive in *a*, alive and contracted in *b*, dead and contracted in *c*. *G*, pus-corpuscles of a good constitution; the bioplasson coarsely granular, alive in *a*, alive and contracted in *b*, dead and contracted in *c*. *M*, pus-corpuscle of a middling good constitution; the bioplasson less coarse, with a compact nucleus; alive in *a*, amœboid in *b*, dead in *c*. *P*, pus-corpuscle of a poor constitution; the bioplasson comparatively scarce, finely granular, vesicular nuclei very distinct; alive in *a*, amœboid in *b*, dead and bursted in *c*.

Whenever we meet with pus-corpuscles in a specimen of urine or sputa, or, for instance, with colorless blood-corpuscles in a drop of blood, which exhibit the features here illustrated in a uniform manner, the conclusion as to the general constitution of the individual can be made with certainty. The exclusive presence of pus-corpuscles of the series *P* is a sure sign of a so-called "tuberculous or phthisical" constitution.

Should pus or blood corpuscles of the series *E* be mixed with those of the series *G* and *M*, this means that an originally excellent constitution has become lowered by disease—the more so the greater the number of the corpuscles like those of the series *P*. Persons of a moderately good constitution, broken down by chronic ailments, or by circumstances not favorable to their nutrition, gradually exhibit, mixed with corpuscles of the series *M*, those of the series *P*. The presence of the series *P* admits of longevity rarely, and only under the most favorable external conditions; the more the formations *c* of the series *P* prevail, the surer it is that the death of the individual is approaching.

Many other conclusions as to the significance of the amount of bioplasson present must be postponed, as they are not as yet sufficiently proved. Obviously, these may in the future lead to an important medical achievement in the prevention of disease.

The features I have described as to the stages of development of living matter must be combined with the conclusions just stated, because the plastids of tissues—I am sure of those of bone and cartilage—exhibit, in all stages of development, differences due to differences in general constitution.

V.

THE STRUCTURE OF COLORED BLOOD-CORPUSCLES.

By Louis Elsberg.*

THE discovery of red corpuscles in the blood was one of the first results of microscopical study, over two hundred years ago. Since that time no other constituent of the body has been more frequently examined. Nevertheless, the structure of colored blood-corpuscles has not heretofore been ascertained.

I.

The examination of a small drop of fresh human blood, mixed with a drop of from 40 per cent. to 50 per cent. saturated solution of bichromate of potash, and highly magnified,† reveals in the course of a few hours the following:

Perhaps the first thing noticed is that the colored corpuscles vary in size.

* "Annals of the New York Academy of Sciences," vol. i., 1879.

† My investigations were made with a $\frac{1}{18}$ immersion objective, manufactured by Tolles, of Boston, and a No. 12 immersion made by Vérick, of Paris, either of which, with the eye-piece that was used, magnifies about 1000 times. An exceedingly thin cover having been oiled near the edges, the drop of blood obtained from a pin-prick in the palm of the hand, and transferred on a slide, is mixed with a drop of the solution previously prepared, covered, and without delay placed on the microscope stage. By a 50 per cent. saturated solution, I mean a saturated solution diluted with an equal quantity of distilled water; by a 40 per cent., one containing three-fifths water; by a 60 per cent., one containing two-fifths water, etc.: I always prepare a saturated solution, and then dilute.

Having made a number of measurements, I can state that in every person's blood that I have examined, there are some as small as, or smaller than, the $\frac{1}{3875}$, and in nearly every person's some as large as, or larger than, the $\frac{1}{2767}$ of an inch in diameter (*i. e.*, .00655 and .00917 mm.), with transitional sizes between these. The extremes are sometimes not met with in each field of a drop, nor even in every drop of a person examined; but I have not found any adult of either sex from whose blood the smaller extreme was absent, and only *very few* without the larger. I have repeated the measurements of blood-corpuscles without the addition of the re-agent, both with and without oiling the edges of the covering-glass,—*i. e.*, with and without preventing the ordinarily rapid evaporation,—with practically the same results; drying of course contracts blood-corpuscles, and corresponding variations are observed. Some of the disks are in outline not perfectly circular; by measuring the largest diameter of the largest and the smallest diameter of the smallest disks, the extremes I have met with in one and the same specimen of human blood are, as to the smallest, about the $\frac{1}{6000}$, and as to the largest, the $\frac{1}{2500}$, of an inch (*i. e.*, .00422 and .01016 mm.). If the detached globules, which I shall describe, be counted as blood-corpuscles, there are even still smaller ones. In each specimen of blood, the majority of red corpuscles, however, are of about one size, which differs in different specimens, but is most frequently between the $\frac{1}{3875}$ and the $\frac{1}{3100}$ of an inch (.00655—.00819 mm.), or somewhere about the $\frac{1}{3370}$ of an inch (.0075 mm.). The calculated average of the size of the red corpuscles in a drop—*i. e.*, the arithmetical mean of the measurements—is usually a little higher than the size of the majority of the corpuscles.

A very few, especially the smallest, but occurring exceptionally also among the larger, seem more or less globular; all others are bi-concave disks, the periphery being more shining and thick than the central portion.

So-called "rosette" and "thorn-apple" forms may be seen, either immediately or in the course of a little while. I have often watched the individual corpuscles while these forms, and many others, were being produced; and in Part III. of this communication I shall offer an explanation of their production.

Concentrating our attention upon the shape of the circular disks, we soon find that the round outline of a few (and the same is at times also true of the smooth surface) begins to be made

irregular at one or more points. This occurs in either of two ways, viz.: by indentation and by protrusion; sometimes the one, sometimes the other, first takes place; frequently both appear in different corpuscles at about the same time; occasionally both are met with in the same corpuscles; in different preparations either the one or the other predominates.

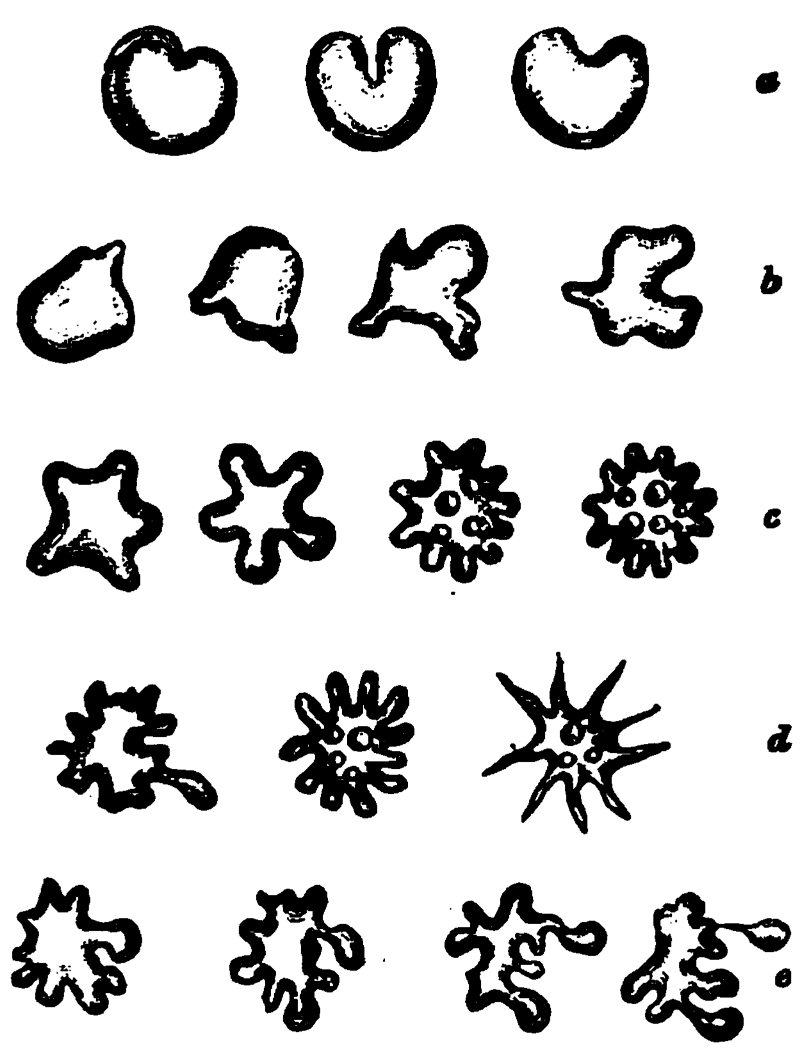

FIG. 21.—SHAPE-CHANGES OF COLORED BLOOD-CORPUSCLES BY INDENTATION.

a, progressing and retrogressing furrowing; *b*, indentations leading to irregular forms; *c*, indentations leading to more or less regular forms; *d*, instances of extreme and exceptional forms, especially the sharp-pointed stellated figure; *e*, four phases of form-change, observed in one corpuscle, with separation of a constricted portion.

First. In from fifteen minutes to an hour a very slight indentation may appear, and gradually deepen, so that the corpuscle be nearly cleaved through; then the clefts may gradually become shallower, so that again a mere indentation is seen; finally, even this may disappear, and the corpuscle be rounded again (see Fig. 21, *a*). Division into two separating halves I have never observed under these circumstances, although I have often watched for it. The furrow of every corpuscle that I have caught nearly cleaved through, either remained stationary, or usually retrogressed to a greater or less extent. The retrogression may stop at any point, and the furrowing again increase; and this going and coming of a cleft, though taking place slowly, may continue for some time, and then stop at any stage of indentation. Sometimes indentations appear at two or more points of the same corpuscle, and in their progress give rise to a great variety of angular, regular, and irregular "rosette," "scalloped," "crenated," "thorn-apple," and "stellate" forms (see Fig. 21, *b*, *c*, *d*). The sharp-pointed ends seen in the last figure of *d* are the extremes met with, and exceptional; usually the ends are plump and rounded. These forms, as well as those of single cleft, after changing backward and forward, either persist or become finally rounded off to a greater or less degree; in some

cases constriction of portions more or less minute occurs, with separation following constriction (see Fig. 21, *e*). Sometimes constricted portions remain attached for a long time by a more or less long and slender pedicle. Transitionally or permanently, in any of the cases mentioned, the most curious and grotesque shapes may be met with. In the cases, too, of constriction and separation, the corpuscles, with the portions attached and unattached, sometimes gradually become rounded off so as to look like a parent globule surrounded by a number of little ones.

Secondly. Usually in the course of half an hour, the protrusion of little round or roundish, more or less light colored, knobs takes place. At first, only very few corpuscles show knobs, and the knobs are extremely small and few in number, say only one, or at most two or three, on a corpuscle; but in the course of an hour or two, more corpuscles protrude knobs, more knobs are protruded from one corpuscle, and the knobs grow larger (Fig. 22, *a*). Occasionally a knob is drawn in again, and the former contour reëstablished. In some instances protrusion and retraction occur repeatedly, so that knobs appear and disappear, or become larger and smaller, very slowly but repeatedly, for some time. Occasionally a knob is pedunculated, and sometimes becomes detached from the corpuscle, while, on the other hand, some knobs are quite sessile.

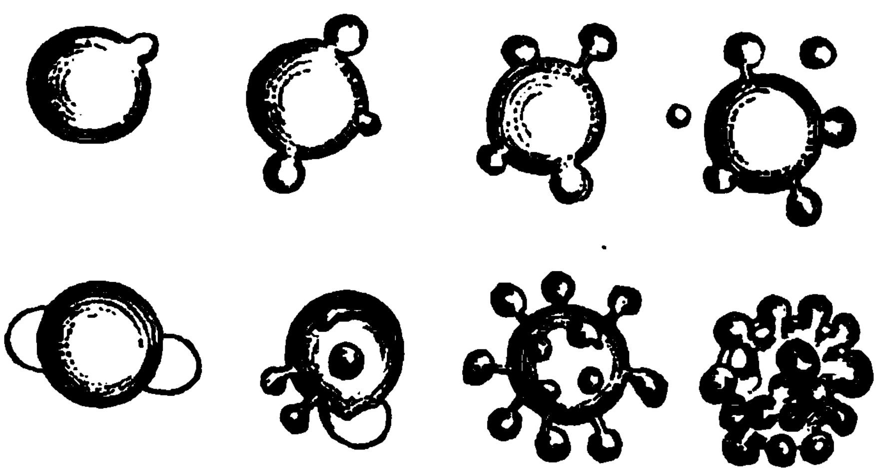

FIG. 22.—KNOB-FORMATION, PRINCIPALLY BY PROTRUSION.

a, Nos. 1 and 2, progressive and retrogressive protrusion; No. 3, one pedunculated and three sessile knobs; No. 4, detachment of two knobs; *b*, protrusion of knobs at the periphery and on the surface; in No. 3, the knobs surround the whole body of the corpuscle; and in No. 4, they are still more numerous.

I have measured portions detached in either of the two ways described, and found them to vary from the $\frac{1}{30000}$ to the $\frac{1}{7500}$ of an inch (.00084—.00338 mm.). All except the very largest may usually be seen in constant oscillatory (molecular) movement, and, unless entangled between larger stationary corpuscles, easily moving across the field (the latter probably caused by minute variation from absolute equilibrium level of the microscope stage).

In some dentated or so-called "mulberry" forms, knobs or small eminences protrude from the face of the disk, which may

give to the inexperienced observer the impression of granules; but proper focusing corrects this impressi shows the knobbed surface. (Fig. 22, *b*).

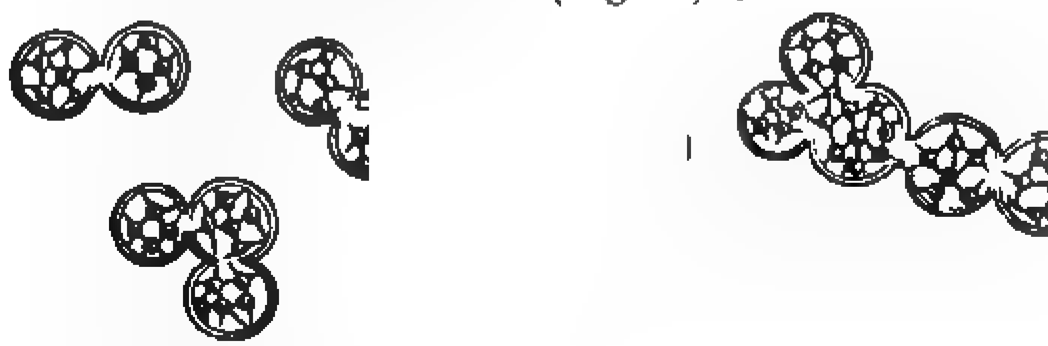

FIG. 23.—COALESCENCE OF TWO OR MORE CORPUSCLES, GIVING CHAINS AND IRREGULARLY SHAPED COMPOUND BODIES, WITH WORK STRUCTURE VISIBLE.

In addition to the protean changes in shape initiate dentation and protrusion, there are still others occasion with, due to combination or coalescence of two or m puscles. In the course of twe hours or more—though this in by far the smaller number arations of blood examined— more adjacent colored bl puscles may, with a larger or portion of their periphery and form compound bodies times chains or other strange (Fig. 23.)

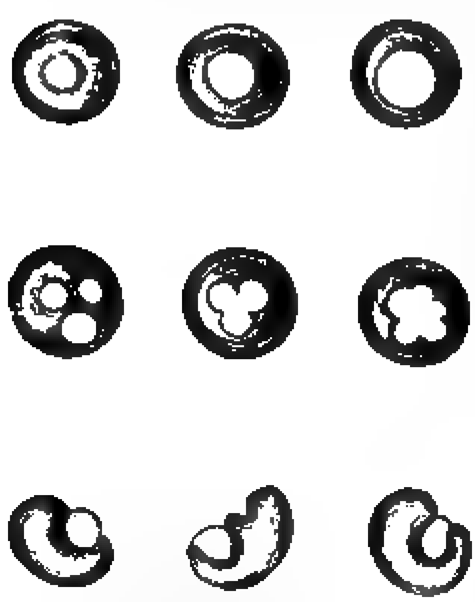

FIG. 24.—VACUOLED CORPUSCLES.

In the upper line are seen three corpuscles, each with a different sized central vacuole, in the middle line, the first figure shows three vacuoles in one corpuscle, these vacuoles are represented in the second figure to be close together, and in the third figure, the separating walls of apparently five vacuoles have broken down, and one irregularly shaped larger vacuole is seen. The lower line shows the appearance of vacuoled corpuscles seen on edge.

Almost immediately on beir for examination, a very few blood-corpuscles show a light vacuole. In the course of the e tion, a number of vacuoles, e different sizes or all of the sa may appear in a corpuscle. a vacuole is round or roundis may assume various irregula —some of which may perha resulted from a union of seve the breaking down of the se walls. (See Fig. 24. The thr figures show appearance of vacuoled corpuscles seen o Vacuoles sometimes persist, and sometimes, after a lo

shorter continuance, suddenly disappear. They are either empty or else contain one or more granules.

Soon after the corpuscles are studied, sometimes from the first, a difference is noticeable as to the intensity of their coloration; some are paler than others. Gradually a larger number of corpuscles become pale, and the degree of paleness, too, increases. There is a great difference in respect to the rapidity of "paling" of colored corpuscles, in blood taken from different persons, even in blood of the same person taken at different times, and with different strengths of the admixed solution of bichromate of potash.

Usually, in blood of healthy persons, examined as I have described, in about an hour from the time the drop of blood is placed on the slide, a few of the corpuscles that are least deeply colored appear to have become somewhat granular in their interior. Focusing shows that this is not the optical illusion alluded to in the case of knobbiness of the surface.

Soon the granules or dots seem more distinct; short, conical thorns, or more delicate spines, appear to issue from one or two of the largest of them; and, on close inspection and focusing, some appear to be connected by irregularly concentric filaments. In the course of five minutes more, a complete net-work is distinctly seen in the interior of one or more corpuscles, and what at first appeared to be granules turn out to be thickened points of intersection of the threads forming this reticulum. These points or dots are irregularly shaped, and vary in size. (See Fig. 25.)

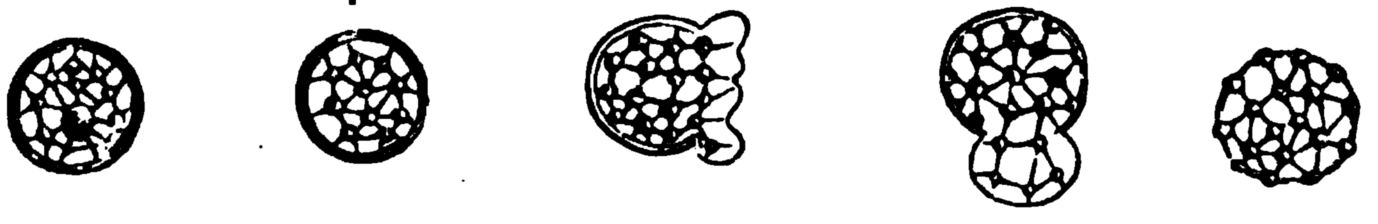

FIG. 25.—THE STRUCTURE OF FIVE COLORED BLOOD-CORPUSCLES.

In the first, there is seen an encircling band of uniform thickness, in which are inserted numerous threads of a net-work; a number of knots are in the interior, which are seen to be the points of intersection of threads constituting a net-work; in the lower portion of the disk there is a larger knot, which may be called a nucleus. In the fifth corpuscle the complete net-work structure is best seen; in this corpuscle there is seen at the periphery, instead of an encircling band, a number of knots united by threads, having the appearance described as beads, each a little separated from its neighbors on the string. The second corpuscle shows the net-work and encircling band, as the majority of corpuscles show them. In the third, a lighter band is seen, and an irregular flap, produced by either indentation or protrusion, or both. The fourth exhibits a large flap or knob at its lower portion, with a stretched or extended net-work.

Radiary threads of the net-work terminate at the periphery of the corpuscle, either with thickened ends connected by threads

—giving an appearance of unevenness to the outer boundary, as though it were constituted by a wreath of beads, each bead separated from its neighbors on the string—or, far more frequently, with terminal points lost in an encircling band of a uniform thickness, often greater than either the interior threads or most points of intersection. From this appearance, as well as that of the so-called "ghosts," to be presently described, it is not to be wondered at that careful observers have ascribed to colored blood-corpuscles the possession of an investing membrane.

As the "paling" progresses, an increasing number of corpuscles show the interior net-work, essentially as I have just described, and identical in construction with the net-work discovered by C. Heitzmann in amœbæ, colorless blood-corpuscles, and other living matter of the body, a discovery which I communicated to the American Medical Association more than three years ago.

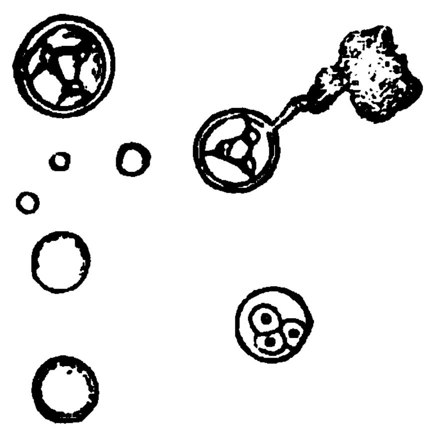

FIG. 26.—THE FINAL PHASES OF COLORED BLOOD-CORPUSCLES TREATED WITH AN APPROPRIATE SOLUTION OF BICHROMATE OF POTASH.

In the upper left-hand figure there is a double-contoured ring, with irregularly massed matter, showing traces of a net-work; in the lower right-hand figure this is less distinct; and in the two lower left-hand figures are represented two so-called "ghosts"; above these there is detritus—*i. e.*, two or three detached portions; and to the right-hand upper figure there is attached a mass which has apparently been extruded.

Gradually an interior net-work structure becomes visible in nearly all the corpuscles in the field, except the smallest, which appear more or less compact; and occasionally a corpuscle is met with having a central, or slightly eccentric, dot of such relatively large size that it might be interpreted as a nucleus. Some movement takes place in the net-work; for sometimes the threads change in length, and perhaps in thickness, and the dots change their position and their size.

In the course of another half-hour or hour, the net-work becomes less distinct in the palest corpuscles; and in these gradually fades away. Then, for some time, the net-work remains visible in nearly all corpuscles except those that are too pale or too small; vacuoles, one or more, appear in many of the latter; while the former occasionally show indications of irregularly massed matter in their interior, though usually nothing is seen of them but double-contoured rings which have been called their "ghosts" (see Fig. 26). During this time, also, a quantity, sometimes rather large, of detritus accumulates.

It appears as though the net-work is most plain in corpuscles that have suffered either not at all or but little from detachment of a portion of their substance. The active changes of indentation and protrusion have usually disappeared in a large number of corpuscles, by the time "paling" has sufficiently progressed to render the interior structure visible. As before stated, some corpuscles permanently retain scalloped and knobbed forms, while the majority are finally more or less rounded off; but the play of changing shape of many corpuscles is going on at the same time that this net-work is seen.

After a while, further "paling" stops, and the net-work structure of all corpuscles which show it, remains visible indefinitely long.

Blood-corpuscles, from hemorrhage in the bladder, in the urine of the late Dr. H****y, preserved with some bichromate of potash, still show the net-work after three years.

Specimens of blood taken from different individuals exhibited all the phenomena described, but with some slight differences among each other as to the order and time of appearance.

A 40 per cent. saturated solution of bichromate of potash, admixed with the blood, was found entirely satisfactory for the demonstration of all the phenomena; and some variation of strength—*i. e.*, between the limits of a 35 per cent. and a 50 per cent. saturated solution—made no appreciable difference.

Of other solutions of bichromate of potash, it is sufficient to state the following:

With a 30 per cent. saturated solution, the phenomena are also to be seen, but appear more slowly, and quite a number of corpuscles usually remain more or less unpaled.

With a 20 per cent. saturated solution, the changes proceed still more slowly; comparatively few indentations occur; the net-work of the majority of corpuscles is visible after the lapse of twenty-four hours, but many remain entirely unaffected.

With a 10 per cent. saturated solution, vacuolation appears, also a little changing indentation and protrusion, but not sufficient paling to render the net-work visible even after several days.

With a 60 per cent. saturated solution, the majority of the corpuscles had already become pale by the time the specimen was in place for examination. Some showed interior net-work, some only double-contoured rings. Protrusions were seen,

especially in the corpuscles not much paled; in one instance, a pale ring was also seen with a large pedunculated protrusion (Fig. 26). During two hours, changes of scalloping and of knobs took place faster than is usual with blood mixed with a 40 per cent. or 50 per cent. saturated solution, but they could not be followed so distinctly. Extreme paling rapidly proceeded, and much detritus filled the field, with only very few compact globules.

With a 90 per cent. saturated solution, the process of scalloping was completed in twenty minutes; and in thirty minutes a net-work was visible in a few roundish corpuscles, surrounded by masses of granular detritus. In addition, a large number of "ghosts" could be seen. Here and there a "ghost" would show a faint net-work.

With a saturated solution added undiluted, the net-work was after one hour visible in some corpuscles, but most of them were destroyed; of a few left intact, some looked homogeneous, and some vacuoled. The field was full of faint, double-contoured rings and a large quantity of granular detritus.

The net-work structure of colored blood-corpuscles is visible also in anatomical preparations which have been kept for a length of time in Müller's fluid.

In some of my examinations, especially the earlier, I used the heated stage; but as the phenomena described were seen at the ordinary temperature of a well-warmed room, I deem it best not to say anything here of variations of temperature.

In this communication I omit the mention, also, of the remarkably varying amount of fibrine threads seen in different preparations of blood; nor do I enter at length into the question of "detritus formation," or whatever else one may interpret as the appearance in the field of an increasing number of free granules, and granular masses or plaques.*

In addition to human colored blood-corpuscles, I have examined those of lower animals. Essentially the same intimate structure as that which I have described exists in all. As examples, I will quote from my note-book a few words referring to the examination of the colored blood-corpuscles of the ox and the newt—the one an example of the unnucleated, the other of the nucleated corpuscles.

* Max Schultze, who saw some of these granules and granular plaques in healthy blood, prefers the designation "granule formation," as being noncommittal.—*Archiv für Mikroskopische Anatomie*, vol. 1, p. 38.

A drop of fresh ox-blood, mixed with a 50 per cent. saturated solution of hromate of potash, and highly magnified (Tolles's $\frac{1}{12}$ immersion) exhibited, hin twenty minutes, vacuolation beginning in several red corpuscles. thin forty minutes, knobs were protruded, though not copiously. In the rse of an hour, "paling" proceeded regularly, so that the net-work became ible in some, and within two hours in a large number, of the corpuscles. ter three hours the net-work, the note-book says, was very distinct in any corpuscles, with some detritus and a few "ghosts." Twelve hours ter, about one-half of the whole number of corpuscles showed the reticulum, hile the other half were either vacuoled or unchanged. No further change as observable for two days. After the third day, some few corpuscles, perhaps, that had not shown the net-work structure before, now did; but the paled ones had become too pale to do so, except a very few which showed it finally. The rest had become "ghosts," with much detritus. A week later, nearly all the corpuscles that had exhibited the net-work had become "ghosts," only in a very few of which faint traces of the reticulum could be made out. The rest were still unchanged, as on the first day, and remained so as long as the specimen was kept.

The red blood-corpuscles of the newt, examined in a 50 per cent. saturated solution of bichromate of potash, into which a drop of the blood from the freshly cut tail had been allowed to fall, presented peculiar changes of shape, consisting mainly in contractions of the body around the nucleus.

The nuclei always exhibited the net-work structure, either perfect, and more distinct than in specimens unmixed with the solution, or, when the nucleus was swelled to double or treble its original size, with the net-work torn. Just as in the case of the colorless corpuscles, there were seen two kinds of red corpuscles, finely granulated and coarse granular, the granules always being the points of intersection of the threads of the net-work. In both kinds, the body as well as the nucleus exhibited the reticulum structure. The net-work of the body and that of the nucleus were connected by fine threads passing through the nuclear envelope. In many instances the body was reduced, either to two polar flaps, bulging from each side of the nucleus, or to one flap, more or less colored, at the side of the nucleus; in other instances, it was uniformly contracted around the enlarged nucleus.

Many colored corpuscles contained vacuoles, in varying number, which were either empty or traversed by an exceedingly delicate, apparently stretched, reticulum, or else contained irregular accumulations of matter with remnants of the net-work.

II.

My observations as to amœboid movements of colored blood-corpuscles, as well as to varieties of size and shape,—observations

which were really only incidental while investigating the structure, the main object of my researches—have been anticipated by previous investigators. One saw, and reported as an extraordinary finding, one or more forms or active form-changes like those I have described; another others; some a far greater number than I. "*Fehlt leider nur das geistige Band.*" The band which connects and explains the phenomena observed is the discovery of the structural arrangement.

In the following historical sketch of points bearing on my observations, I shall refer to a few only of the legion who have made colored blood-corpuscles the subject of their investigation.

More than a hundred years ago, William Hewson, after asserting that the red corpuscles are of different sizes in different animals, added: "I have likewise observed that they are not all of the same size in the same animal, some being a little larger than others,"* etc. Hewson's editor, Gulliver, who has made a very large number of measurements of red blood-corpuscles of different animals, and is "our highest authority upon the subject," said of his own elaborate tables: "We are only speaking now of the average size, for they vary like other organisms; so that in a single drop of the same blood you may find corpuscles either a third larger or a third smaller than the mean size, and even still greater extremes"; † and more recently,‡ "But as I have long since shown, the corpuscles in one species of the vertebrate class, as seen in a single individual thereof, vary so much in size that their average dimensions cannot be determined with absolute precision; and were this fact kept in view much needless discussion might be spared."

Beale, also, long ago called attention to the fact that "corpuscles may be found which are not more than the fifth or sixth of the size of an ordinary blood-corpuscle."§ Again: "The red corpuscles vary in size, and more than is usually supposed"; ‖ and again: "It is generally stated that the red blood-corpuscles of an animal exhibit a certain definite size; but it will be found that they vary extremely, so that corpuscles exist of various dimensions."¶

Welcker ** found in the blood of Dr. Schweigger-Seidel colored blood-corpuscles as small as .0051, and as large as .0085 mm. Altogether, the mini-

* "Philosophical Transactions," vol. lxiii., Part II., p. 320 (read June 24, 1773). The works of William Hewson, F. R. S., Edited, with an Introduction and Notes, by George Gulliver. F. R. S., London. Published by the Sydenham Society, 1846; p. 234.

† "Lectures on the Blood of Vertebrata." *Medical Times and Gazette*, vol. ii. of 1862. p. 157.

‡ "Comparative Photographs of Blood-disks." *Monthly Microscopical Journal*, November, 1876, p. 240.

§ "Archives of Medicine," vol. ii. (No. 8), p. 236, and *Quarterly Journal of Microscopical Science*, April-May, 1861; p. 249.

‖ "Observations upon the Nature of the Red Blood-corpuscles." Transactions of the Microscopical Society of London (read Dec. 9, 1863), vol. xii., N. S., p. 37. *Quarterly Journal of Microscopical Science*, Jan., 1864.

¶ "The Microscope in its Application to the Practice of Medicine," third edition. Republished in Philadelphia, 1867; p. 170.

** "Grösse, Volum und Oberfläche und Farbe der Blutkörperchen bei Menschen und bei Thieren." Zeitschrift für rationelle Medicin, S. iii., vol. xx. (1863), p. 237.

mum measurement recorded in his table is .0045 mm., and the maximum, though not in the same specimen, .0097 mm. He remarks: "I have always, both in animals and in man, found the transverse diameter of the blood-corpuscles of one and the same individual vary from one-fourth to one-half of the mean measurement; and it appears that all the sizes lying between the two extremes are present in tolerably equal numbers, with the exception of the smallest corpuscles, which occur for the most part singly and at intervals." *

Max Schultze distinguished in his own and other persons' healthy blood two forms of colored corpuscles, viz.: globular and disk-like; the globular, few in number, vary from .005 to .006 mm. in size; and from these there are gradual transitions to the ordinary disks, which measure from .008 to .010 mm. †

The smallest colored corpuscles which Klebs reported ‡ having found in his own blood varied from .0058 to .0066 mm.; but in blood from the corpse of a leucæmic child he observed a few as small as .00416 mm.

Woodward said: "The truth is that not only do the individual corpuscles in every drop of blood vary considerably in size, but as might be anticipated from this very fact, the average size obtained by measuring a limited number of corpuscles (50 to 175, still more in the case of but 10 to 50, as usually practiced), varies considerably, not only between different individuals, but also between different parts of the very same drop of blood." Both the maximum and the minimum which he found—viz.: the 396 millionths and the 216 millionths of an inch, or .01005 and .00548 mm.—were present in the same field of one drop. §

Berchon and Perrier ‖ state that the colored blood-corpuscles of the fœtus and the newly born are on an average smaller than those of adults. The extremes given are: minimum, .0031 to .0062 mm., and maximum, .0091 to .0093 mm.; but they do not mention that the extremes occurred in one and the same case. More recently, Perrier ¶ measured blood-corpuscles of thirty-five individuals of different ages, and found that those of .010 mm. were very frequent in the first days after birth, while later they occurred much more rarely. After the first year, blood-corpuscles measuring .0093 mm. were rarely present in greater proportion than ten in a hundred; and in adults often absent. Such of .0043 mm. occurred most often in the aged and in children. The diameter of the great mass at every age varies from .0050 to .0087 mm.; within these limits those of .0075 mm. are most frequent and never absent. The form of the smaller is more or less globular; the larger are flattened.

* Cited by Woodward, "On the Similarity between the Red Blood-corpuscles of Man and those of certain other Animals, especially the Dog: considered in connection with the diagnosis of Blood-stains in criminal cases." *American Journal of Medical Sciences*, Jan., 1875. *Monthly Microscopical Journal*, Feb. 1, 1875, p. 69.

† "Ein heitzbarer Objecttisch und seine Verwendung bei Untersuchungen des Blutes." Archiv für Mikroskopische Anatomie, vol. i. (1865), p. 35.

‡ "Ueber die Kerne und Scheinkerne der rothen Blutkörperchen der Säugethiere." Virchow's Archiv für pathologische Anatomie und Physiologie und für Klinische Medicin: vol. xxxviii. (1867), p. 195.

§ "The Application of Photography to Micrometry, with special reference to the micrometry of blood in criminal cases." Transactions of the American Medical Association, vol. xxvii. (1876), p. 303–315.

‖ "Note sur les globules du sang chez le fœtus." Bordeaux Médical., p. 123 and 237; Canstadt's Jahresbericht for 1875, I., p. 46.

¶ "Sur les variations du diamètre des globules rouges du sang dans l'espèce humaine, au point de vue de l'espertise légale." Compt. Rendus, tom. 84 (1877), No. 24, p. 1404.

According to Hayem,* the red blood-corpuscles in the newly born are much less uniform in size than in adults; corpuscles larger than the largest and smaller than the smallest adult corpuscles occur comparatively often. The size varies between .00325 and .01025 mm. Hayem also calls attention † to the still smaller ones — measuring only .002 mm. — which he considers young and growing blood-corpuscles, so-called hæmatoblasts. He asserted having observed all transition sizes between these and the largest. He found hæmatoblasts increased whenever, under physiological or pathological conditions, a reparation of blood occurs — *e. g.*, he found them more abundant in children than in adults, and more abundant during menstruation, and after losses of blood, also during reconvalescence after acute diseases.‡

Netsvetzki reported § having found minute corpuscles moving in all directions, as constant constituents of normal human blood. [Although my observations as to the diversity of size of colored blood-corpuscles refer to healthy blood, I will not omit to mention here that Vanlair and Masius having, in the blood of a patient who had symptoms of interstitial hepatitis, found a number of small globular corpuscles, gave them the name of microcytes, and called the patient's disease "microcythæmia," which they considered to be a peculiar alteration of the blood. ‖ Cases of so-called microcythemia have since been reported by Litten, in a tuberculous individual; ¶ by Osler in pernicious anæmia **; and by Lepine and Germont in cases of cancer of the stomach.†† Soernsen distinguished in disease between oligocythemia, in which the number of red blood-corpuscles is diminished, achroiocythemia, in which their richness in coloring matter is diminished, and microcythemia, in which their size is diminished. In a case of chlorosis observed by him, the average size of the colored corpuscles was found to be only .0045, instead of the normal .006 to .0075 mm.‡‡

Hicks §§ found in the fluid from an ovarian cyst small, transparent, colorless, globular bodies, which had been detached from red blood-corpuscles, and which were of a diameter of about the $\frac{1}{10000}$ of an inch.

Laptschinsky reported ‖‖ finding very small corpuscles, only one-third as

* "Des caractères anatomiques du sang chez le nouveau-né pendant les premiers jours de la vie." Compt. Rendus, tom. 84 (1877), p. 1166.

† "Sur la nature et la signification des petits globules rouges du sang." *Ibid.*, No. 22, p. 1239.

‡ "Note sur l'évolution des globules rouges dans le sang des vertébrés ovipares." Compt. Rendus, tom. 85, No. 20, p. 907-909. "Sur l'évolution des globules rouges dans le sang des animaux superieurs" (verteb. ovipares). *Ibid.*, No. 27, p. 1285.

§ "Zur Histologie des Menschenblutes. Kleine sich nach allen Richtungen hin bewegende Körperchen als constante Bestandtheile des normalen Menschenblutes." Centralzeitung für die Medicinischen Wissenschaften, 1873, No. 10.

‖ "De la Microcythemie, Bruxelles, 1871; 101 pp.

¶ "Aus der Klinik des Herrn Geh. Rath. Prof. Frerichs, "Ueber einige Veränderungen rother Blutkörperchen." Berliner Klinische Wochenschrift; 1877, No. 1.

** "Ueber die Entwickelung von Blutkörperchen in Knochenmark bei perniciöser Anæmie." Centralblatt für die medicinischen Wissenschaften; 1877, No. 28; 1878, No. 26.

†† Note sur la presence temporaire dans le sang humain d'un grand nombre de globules rouges tres petits (microcytes)." Gazette Medicale de Paris; 1877, No. 18, pp. 218 and 219; and "Note relative a l'influence des saignées sur l'apparition dans le sang humain des petits globules rouges (microcytes)." *Id.*, No. 24, p. 296.

‡‡ "Undersogelser om Antallet af rode og hvide Blodlegemer under forskjellige physiologiske og pathologiske Tilstande." Inaugural Dissertation, Kopenhagen; 1876, 236 pp.

§§ "Observations on Pathological Changes in the Red Corpuscle." *Quarterly Journal of Microscopical Science*, vol. xii. (1872), p. 114.

‖‖ "Zur Pathologie des Blutes." Centralblatt f. d. med. Wiss., 1874, No. 42, p. 658.

large as the normal ones, in conditions of the body accompanied with high fever, especially in infectious diseases.

Hayem has come to the conclusion* that in anæmia the blood-corpuscles are in general smaller than in normal conditions; but that the extremes which are met with are greater, viz.: .0022 and .010 to .014 mm.

Piper found in a case of "ulcerated scrotum and inflamed testicle, with apparently tuberculous deposit in the gland," on one and the same slide, specimens which measured $\frac{1}{4083}$ of an inch; while on other parts of the same slide alike extensive fields of corpuscles which measured only a fraction less than the classic $\frac{1}{3200}$ of an inch.†

Ponfick,‡ Osler,§ and Obermeier‖ have reported other abnormities.]

According to Richardson,¶ the variations above and below the standard size of corpuscles from any particular animal are comparatively slight in fresh blood, as proved by the following experiments, made with his $\frac{1}{16}$ inch objective, which gives with the micrometer eye-piece an amplification of 3700 diameters. When thus magnified, the human red blood-disks appeared about an inch and one-eighth in diameter, so that even slight differences in their size could be accurately measured. Among one hundred red corpuscles freshly drawn from five different persons, the maximum and minimum diameters in parts of an inch were as follows:

Twenty	from	a white male	aged	30,	maximum	1-3231,	minimum	1-3500
"	"	" "	"	38,	"	1-3281,	"	1-3529
"	"	" female	"	44,	"	1-3249,	"	1-3500
"	"	an African "	"	50,	"	1-3182,	"	1-3559
"	"	a white male	"	8,	"	1-3231,	"	1-3500

Moreover, the smallest red disks of man, as usually met with in mechanically unaltered blood, whether dry or moist, are, according to him, larger than the largest corpuscles of an ox, and *a fortiori* of a sheep.

More recently,** he measured corpuscles of individuals of fourteen different nations, one hundred of each. Of the 1400 corpuscles measured, the average was $\frac{1}{3224}$ (.007878 mm.), the maximum $\frac{1}{2777}$, and the minimum $\frac{1}{4000}$ of an inch; 1158, or 83 per cent., measured between $\frac{1}{3448}$ and $\frac{1}{3030}$ of an inch in diameter, and consequently under a power of two hundred would appear about the same magnitude; the total number of corpuscles of minimum measure was only six, or less than one-half of one per cent.; and the total number which measured the maximum was ten, or less than one per cent.

* "Des Caractères Anatomiques du Sang dans les Anemies." Comptes Rendus, tome 83 (1876), pp. 82, 85, p. 152, p. 230.

† "Contraction of Blood-corpuscles through the action of Cold." *New York Medical Journal*, March, 1877, p. 246.

‡ "Ueber das Vorkommen abnormer Zellen im Blute von Recurrenskranken." Centralblatt f. d. med. Wiss., 1874, No. 25.

§ "An Account of Certain Organisms occurring in the Liquor Sanguinis." *Monthly Microscopical Journal*, September, 1874, p. 141.

‖ "Vorkommen feinster, eine Eigenbewegung zeigender Fäden im Blut von Recurrenskranken." Centralblatt für die med. Wiss., 1873, No. 10. Confirmed by Laptschinsky. *Id.*, 1875, No. 9, p. 84.

¶ "On the Value of High Powers in the Diagnosis of Blood-stains." *American Journal of the Medical Sciences*, July, 1874; and *London Monthly Microscopical Journal*, September, 1874, p. 135.

** "On the Identity of the Red Blood-corpuscles in Different Races of Mankind." *American Journal of the Medical Sciences*, January, 1877, p. 112.

All this is very remarkable, unless he measured mainly the majority, or average-sized corpuscles. He made some selection, for he tells us: "Instead of measuring all corpuscles, deformed or otherwise, in two directions, as proposed by Dr. Woodward (*Phila. Medical Times*, vol. vi., p. 457), I prefer to determine the size of unaltered, *i. e.* circular, corpuscles *only*"; further, "I cautiously avoided recording those which manifested even slight departures toward an oval form," but, on the other hand, "to secure the most infallible accuracy for my deductions, as the preparation was moved along, I measured *every isolated circular red disk* which came into the field of the microscope."

In the year 1761, Padre Jo. Maria de Torre, of Naples, made a present to the Royal Society of London of four spherical glasses for the microscope, made by himself, of which the diameters and magnifying powers were said to be as follows:

	Diameter.	Magnifying Power.		
1.	Near 2 Paris points.	640 times, and upward, in diameter.		
2.	1 Paris point.	1,280 "	"	"
3.	1 " "	1,280 "	"	"
4.	Half a Paris point. ($\frac{1}{144}$ of an inch.)	2,560 "	"	"

Sir Francis Haskins Eyles Stiles, at the time in Naples, through whom the presentation was made, wrote several letters, in which he communicated Father de Torre's direction for the use of the glasses, as well as an account of some observations on the human blood, made by him, together with Torre, during July and August, 1761, and read before the Society during November, 1765. They saw in the blood-globules the central depression, which had not theretofore been observed, and which carried with it so strongly the appearance of a perforation that they concluded the corpuscles to be rings. They also thought the rings to be articulated ("the transverse lines at the joints being very distinguishable").* As to their shape, "the figure of the rings, where they were free and in their natural state, was circular; but where they were so crowded together as to compress one another in their passage, they assumed a variety of different figures, although they generally restored themselves to a circular figure again, unless broken by the compression, which frequently happened, and then the broken parts floated separately; or, if they opened at a single joint only, the whole of the ring would float along, varying its figure occasionally from that of a portion of a circle, which it would first assume, to a straight line, an undulated one, or some other accidental incurvature." †

Hewson ‡ declared the so-called globules in the blood of man and all animals to be disks—"in reality, flat bodies," "as flat as a guinea." The dark spot in the middle, which Father de Torre had taken for a hole, he found "was not a perforation, and therefore that they were not annular." He denied that they were jointed, and inferred "they are not fluid, as they are commonly

* "An Account of some Microscopic Observations on the Human Blood." Philosophical Transactions, vol. lv. (1765), p. 254.

† *Ibid.*, p. 256.

‡ "On the Figure and Composition of the Red Particles of the Blood, commonly called the Red Globules." Philosophical Transactions, vol. lxiii., Part II. (1773), pp. 303–323.

ieved to be; but, on the contrary, are solid; because every fluid swimming another, which is in larger quantity, if it be not soluble in that fluid, comes globular." He also observed changes of shape; for, speaking of the od-corpuscles of a lobster, he said: "But there is a curious change proceed in their shape by being exposed to the air; for, soon after they are ceived on the glass, they are corrugated, or from a flat shape are changed to irregular spheres, as is represented in Plate XII., No. 12";* and on rning to the plate we find represented "angular," "rosette," and "stelated" forms. He was the first who likened the appearance of corpuscles, with their external surface corrugated, to that of small mulberries.†

It would be impossible for me, as well as useless, to give a list of all those who have described changes of form in red blood-corpuscles since Hewson's time. Different shapes—and some of them far more curious and irregular than those I have described—have been observed, under many physiological and pathological conditions, as well as on subjecting the blood to the action of various chemical and physical agencies. Text-books and monographs give sufficient information on this point, especially the article on the blood by Alexander Rollet, in Stricker's "Handbuch der Lehre von den Geweben des Menschen und der Thiere," which has been translated by Henry Power and published by the London New Sydenham Society, and which has been republished in this country.‡

Since that article was written the following observations have been made:

Langhans,§ in experiments on rabbits, saw, in extravasated blood, red corpuscles with numerous fine projections, and in pigeons' red blood-corpuscles, also, observed morphological changes.

Lieberkühn‖ described remarkable form-changes in the red corpuscles of the blood of salamanders and of pikes.

Wedl¶ observed changes of shape in human and frogs' red blood-corpuscles on adding a drop of concentrated aqueous solution of pyrogallic acid to a drop of fresh blood.

Ray Lankester** found in his own healthy blood, in addition to the ordinary biconcave forms, "thorn-apple" and "single and double watch-glass" forms. In the two latter there is, when the corpuscle is seen on edge, instead of a concavity, a convexity on either one or both sides. He also described and figured varieties of shape in both human and frogs' colored blood-corpuscles subjected to the action of various re-agents. Of these I shall cite, later on, the effects of very dilute ammonia gas and acetic acid vapor.

Braxton Hicks†† observed colored blood-corpuscles of various shapes in fluid from an ovarian cyst, and in blood in other pathological conditions.

* *Ibid.*, p. 321. Opus posthumum, pp. 19, 20; Collected Works, edited by Gulliver, *cit.*, p. 234.

† *Ibid.*, p. 313, etc.

‡ "A Manual of Histology." By Prof. S. Stricker. American translation edited by Albert H. Buck. New York: Wm. Wood & Co., 1872.

§ "Beobachtungen über Resorption der Extravasate und Pigmentbildung in denselben." Virchow's Archiv, vol. xlix. (1870), pp. 66-116.

‖ "Ueber Bewegungserscheinungen der Zellen." Schriften der Gesellschaft zur Beförderung der gesammten Naturwissenschaften zu Marburg, vol. ix. (1870), p. 335.

¶ "Histologische Mittheilungen: Ueber die Einwirkung der Pyrogallussäure auf die rothen Blutkörperchen." Sitzungsberichte der Wiener Akademie der Wissenschaften, vol. lxiv. (1871), 1 Div., p. 405.

** "Observations and Experiments on the Red Blood-corpuscle, chiefly with regard to the Action of Gases and Vapours." *Quarterly Journal of Microscopical Science*, October, 1871, p. 361-387.

†† Observations *cit. Quarterly Journal of Microscopical Science*, vol. xii. (1872), p. 114.

Huels * described frogs' red blood-corpuscles acted on by carbolic acid.

Faber † observed, in the urine of a patient with Bright's disease, colored blood-corpuscles of a great variety of different shapes, some of which showed him phenomena of contractility and amœboid movement, "very similar" to those of colorless blood-corpuscles.

Hüter ‡ reported seeing in the capillaries of the frog lung a few red blood-corpuscles adhere to the sides by means of a drawn-out pedicle, with half the body on each side, having a saddle-bag-like shape ("*zwergsackähnlich*").

Laptschinsky described and figured § the effects of various re-agents, among them aniline blue, magenta, and tannin, on the red blood-corpuscles of triton and man. He confirmed and enlarged the older observations of Roberts.‖ Laptschinsky ¶ also described some variations of shape which he met with on examining human blood in different diseases.

Arnold, ** in the course of his observations on diapedesis of colored blood-corpuscles after ligating the median vein of the frog's tongue, saw that in the various phases of transit these corpuscles assumed various shapes, sometimes pear-shaped, with slender stem, sometimes caudated, oval, etc. Similar shapes have under similar circumstances been described by others.

Hiller †† refuted the supposition of Hüter (II. Deutscher Chirurgen Congress, April 18, 1873), that the stellate and thorn-apple forms of red blood-corpuscles are due to immigration of monads into the substance of the corpuscles. He found such forms in blood during febrile and non-febrile diseases; they were absent in some cases in which large quantities of monads had been injected into the blood of animals; and he observed in many cases their development directly under the microscope.

Rommelaere ‡‡ observed in various diseases changes of shape of the red blood-corpuscles.

Landois §§ saw corpuscles assume, before their dissolution, a spherical form with exceedingly fine points.

Ebert,‖‖ Böttcher,¶¶ Fuchs,*** and Schmidt ††† have reported variations of the ordinary shape. The latter has also called attention to the fact that human red blood-corpuscles, seen in exact profile and closely examined, are repre-

* "Wirkung der Carbolsäure auf rothe Froschblutkörperchen." Inaug. Dissertation, Greifswalde, 1872, 43 pp.

† "Ueber die rothen Blutkörperchen." Archiv der Heilkunde, 1873, xiv., p. 481-511.

‡ "Ueber den Kreislauf und die Kreislaufstörungen in der Froschlunge." Centralblatt für die Medicinischen Wissenschaften, 1873, No. 6, p. 82.

§ "Ueber das Verhalten der rothen Blutkörperchen zu einigen Tinctionsmitteln und zur Gerbsäure." Sitzungsberichte der Wiener Akademie, vol. lxviii. (1873), Div. III., p. 148.

‖ "On peculiar appearances exhibited by blood-corpuscles under the influence of solution of magenta and tannin." *Quarterly Journal of Microscopical Science*, 1863, p. 170.

¶ "Zur Pathologie des Blutes." Centralblatt für die Medicinischen Wissenschaften, 1874, No. 42, pp. 660 and 661.

** "Ueber Diapedesis." Virchow's Archiv, vol. lviii. (1873), pp. 203-254.

†† "Ueber die Veränderungen der rothen Blutkörperchen nebst Bemerkungen über Microcyten." Centralblatt f. d. Med. Wiss., 1874, Nos. 21, 25.

‡‡ "De la deformation des Globules rouges du Sang." Bruxelles, 1874, 47 pp.

§§ "Auflösung der rothen Blutzellen." Centralblatt f. d. Med. Wiss., 1874, No. 27, p. 419.

‖‖ "Ueber Formveränderungen der rothen Blutkörperchen." Greifswald, 1875.

¶¶ "Ueber einige Veränderungen welche die rothen Blutkörperchen in Extravasaten erleiden." Virchow's Archiv, vol. 69 (1876), p. 295-307. Also in other articles which I quote in this review.

*** "Beitrag zur Kenntniss des Froschblutes und der Froschlymphe." Virchow's Archiv, vol. 71 (1877), pp. 78-107.

††† "The Structure of the Colored Blood-corpuscles of Amphiuma tridactylum, the Frog, and Man." *Journal of the Microscopic Society of London*, May and July, 1878, pp. 66, 68, 110, etc.

sented by two straight and parallel lines, connected at their extremities by two semicircular ones, and not showing merely their central concavity, as usually represented.

The question whether or not colored blood-corpuscles possess an investing membrane has been much discussed. Hewson, who, as I have already stated, showed that these corpuscles are not perforated, contended that the dark spot in the middle, believed by Torre to be a perforation, "is a solid particle contained in a flat vesicle, whose middle only it fills, and whose edges are hollow, and either empty or filled with a subtile fluid."* He detailed the following experiments: "Take a drop of the blood of an animal that has large particles, as a frog, a fish, or, what is still better, of a toad; put this blood on a thin piece of glass, as used in the former experiment, and add to it some water—first one drop, then a second, and a third, and so on, gradually increasing the quantity; and in proportion as water is added, the figure of the particle will be changed from a flat to a spherical shape; . . . it will roll down the glass stage smoothly, without those phases which it had when turning over when it was flat; and, as it now rolls in its spherical shape, the solid middle particle can be distinctly seen to fall from side to side in the hollow vesicle, like a pea in a bladder." He added: "From the greater thickness of the vesicles in the human subject, and from their being less transparent when made spherical by the addition of water, and likewise from their being so much smaller than those of fish or frogs, it is more difficult to get a sight of the middle particles rolling from side to side in the vesicle, which has become round; but with a strong light (these experiments were all made with daylight, in clear weather) and a deep magnifier, I have distinctly seen it in the human subject, as well as in the frog, toad, or skate." Another experiment he describes thus: "If a saturated solution of any of the common neutral salts be mixed with fresh blood, and the globules (as they have been called, but which for the future I shall call flat vesicles) be then examined in a microscope, the salt will then be found to have contracted or shriveled the vesicles, so that they appear quite solid, the vesicular substance being closely applied all around the central piece." Furthermore, "the fixed vegetable alkali and the volatile alkali were tried in a pretty strong solution, and found to corrugate the vesicles."

The vesicular nature of colored blood-corpuscles, thus announced more than sixty years before the publications of Schleiden and Schwann, so perfectly fits into their cell-schema that many suppose that they have originated this view of the constitution of the corpuscles. But in point of fact they have in this respect followed Hewson. According to Schwann,† the red blood-corpuscle is a cell, and consists, like every other cell of the body, of a membraneous envelope, a nucleus, and liquid contents; the credit of the observation of the "rolling around" of the nucleus is given by Schwann to C.

* "On the Figure and Composition of the Red Particles of the Blood, commonly called the Red Globules." Philosophical Transactions, vol. 63, Part II., p. 310 *et seq.* (read June 17 and 20, 1773). "A Description of the Red Particles of the Blood in the Human Subject and in other Animals, being the remaining part of the Observations and Experiments of the late Wm. Hewson." By Magnus Falconer. London, 1777. p. 221 *et seq.*

† "Mikroskopische Untersuchungen über die Uebereinstimmung in Structur und Wachsthum der thierischen und pflanzlichen Organismen." Berlin, 1839, pp. 74, 75.

H. Schultz, who, however, has only repeated and confirmed * the experiment of Hewson.

Although not accepted without some opposition, it was not until the year 1861 that the existence of a cell-wall was positively denied. Beale declared: † "I have never succeeded in seeing the cell-wall said to exist, neither have I been able to confirm the oft-repeated assertions with regard to the passage of liquid into the interior of the corpuscle by endosmose, its bursting, and the escape of its contents through the ruptured cell-wall. When placed in some liquids, many of the corpuscles swell up and disappear; but I have never seen the ruptured cell-walls." He also published observations which he considered "fatal to the hypothesis that each corpuscle is composed of a closed membrane with fluid contents." ‡ Brücke expressed the opinion that the rolling around of the nucleus is illusory, that other phenomena do not conclusively prove the presence of a membrane, and that "the unanimity with which the vesicular nature of blood-corpuscles had for a long time been taught was owing more to the silence of the opponents than to the force of the arguments of the believers." § Vintschgau ‖ and Rollett ¶ also argued against the existence of an investing membrane; and the opinion seemed doomed.

But before the end of the year in which Beale and Brücke contested the existence of an investing membrane, Hensen defended it. ** He reports having observed in the blood of frogs, both in fresh preparations—*i. e.*, in red corpuscles examined without the addition of any re-agent—and in corpuscles placed in various mixtures, especially a solution of sugar, that sometimes the membrane, as a distinct outer contour, is lifted up from the interior contents at one or more points of the circumference, these interior contents being retracted more or less densely upon the nucleus. A few years later, †† Hensen reiterated his conviction as to the presence of a membrane; it is certain, therefore, that Lankester ‡‡ has misapprehended his meaning. Kölliker, who had previously asserted that the red blood-corpuscle possesses "a very delicate but nevertheless tolerably firm and at the same time elastic colorless cell-membrane, composed of a protein substance closely allied to fibrin," §§ continued to uphold their vesicular constitution. ‖‖ Preyer reported that the

* "Das System der Circulation." Stuttgart and Tübingen, 1836, p. 19, *et seq.*

† "Lectures on the Structure and Growth of the Tissues of the Human Body. Delivered at the Royal College of Physicians. Lecture III., April 22, 1861." Archives of Medicine, vol. ii., No. 8 (May, 1861), p. 236. Republished in *Quarterly Journal of Microscopical Science*, vol. i., N. S. (April-May, 1861), p. 240.

‡ "Observations upon the Nature of the Red Blood-corpuscle." Transactions of the Microscopical Society, vol. xii., N. S., p. 37. *Quarterly Journal of Microscopical Science*, Jan., 1864.

§ "Die Elementarorganismen." Sitzungsberichte der Wiener Akademie, vol. xliv., Div. ii., p. 389 (read Oct. 17, 1861).

‖ "Sopra i Corpusculi Sanguigni della Rana." Atti del Instituto Veneto, vol. viii., Ser. iii.

¶ "Versuche und Beobachtungen am Blute." Sitzungsberichte der Wiener Akademie, vol. xlvi. (1862), p. 65.

** "Untersuchungen zur Physiologie der Blutkörperchen sowie über die Zellennatur derselben." Zeitschrift für wissenschaftliche Zoologie, vol. xi., Heft 3 (Ausgegeben Dec. 23, 1861), pp. 253-278.

†† In a foot-note of an article entitled "Ueber das Auge einiger Cephalopoden." *Ibid.*, vol. xv., Heft 2 (April 1, 1865), p. 170.

‡‡ Lankester, in his article on the red blood-corpuscle, in the *Quarterly Journal of Microscopical Science*, October, 1871, already cited, says, p. 366, that Hensen "distinguishes a layer of fluid protoplasm surrounding the coloring matter, by cadaveric alteration of which he believes the supposed membrane of the corpuscle to be formed."

§§ "Manual of Human Histology." Translated and edited by George Busk and Thomas Huxley, London, Sydenham Society, 1854, vol. ii., p. 326.

‖‖ Handbuch der Gewebelehre, 1863, p. 627.

early observation of the rolling nucleus (erroneously ascribed by him, after Schwann, to Schultz instead of to Hewson) agreed with what he himself had seen, and, at least so far as red corpuscles of the blood of salamanders are concerned, positively declared a membrane normally to exist.* As proof of the existence of a membrane, and of its taking no part in the formation of blood-crystals, Bryanowski refers to his success in demonstrating it by means of distilled water. † Owsjannikow says: "To prove with certainty the existence of the membrane is no easy task. Preparations occur which seem to be convincing that there is no membrane; but other preparations show it without the addition of any re-agent. The interior contents retract away from it, so that between it and the yellowish colored contents an empty space remains. Still more distinctly than in pure blood is the membrane seen on the addition of a weak solution of sugar, either without or with admixture of a little alcohol. Then it appears in many, or perhaps in most, of the blood-corpuscles." Furthermore, he describes interior crystallization in which he has seen the membrane pushed out lengthwise by a crystal, and other cases in which "the membrane becomes very distinctly visible as it passes from nucleus to crystal." With high magnifying power, he says, human red blood-corpuscles not seldom show a very delicate membrane; and one of his conclusions is: "In the blood-corpuscles of most animals an independent membrane can be proved to exist, which behaves toward serum, water, etc., differently from the cell-contents, and which occasionally possesses considerable firmness." ‡ Richardson argued § in favor of the same view, mainly on account of experiments upon the gigantic blood-disks of the menobranchus, in which "crystals of hæmato-crystallin were seen to prop out a visible membraneous capsule." More recently, Richardson exhibited before the members of the Section on Biology of the International Medical Congress of Philadelphia, a slide with a colored blood-corpuscle of the amphiuma tridactylum, of which it is reported that "the imperfectly crystallized cell-contents occupy the upper end, while the oval granular nucleus fills the inferior extremity, leaving the membraneous capsule relaxed and wrinkled longitudinally, hanging like part of a half-flaccid balloon between them." ‖ Arloing, as the result of his observations, ¶ ascribed a membrane to red blood-corpuscles. Kollmann, after expressly declaring that when he uses the word membrane in relation to red blood-corpuscles, he means to speak of what may be called an "artefact," *i. e.*, "that apparent membrane which is made visible by the action of reagents," ** discusses the arguments pro and con, and concludes that "the adherents of a membrane have for their opinions at least as many reasons as the opponents." †† He himself believes in "the existence of a membrane in the fresh condition,

* "Ueber amœboide Blutkörperchen." Virchow's Archiv, vol. xxx. (1864), p. 437.

† "Beobachtungen über die Blutkrystalle." Zeitschrift für wissenschaftliche Zoologie, vol. xii., Heft 3 (November 17, 1862), p. 317.

‡ "Zur Histologie der Blutkörperchen." Bulletin de l'Academie des Sciences de St. Petersbourg, t. viii. (1865), pp. 564, 568–570.

§ "On the Cellular Structure of the Red Blood-corpuscle." Transactions of the American Medical Association for 1870, pp. 259-271.

‖ Transactions of the International Medical Congress of Philadelphia, held in 1876. Philadelphia, 1877, p. 488.

¶ "Recherches sur la nature du Globule Sanguin." Compt. Rendus, t. lxxiv. (1872), No. 19, pp. 1256-1259.

** "Bau der rothen Blutkörperchen." Zeitschrift für wissenschaftliche Zoologie, vol. xxiii., Heft 3 (November 18, 1873), p. 467.

†† *Ibid.*, p. 482.

which can be made visible by the action of re-agents by depriving the corpuscle of coloring matter, and which, when it does not become visible, has been destroyed by the re-agent." * According to Böttcher, the outer layer of the same blood-corpuscle is not the same at all times and under all circumstances. He seems to regard the appearance of a distinct membrane as an artificial production; but considers "the cortical layer as the result of a process of development which deprives the blood-cells more and more of their protoplasm, and finally converts them into homogeneous bodies." He, therefore, classes it "with the capsule of cartilage cells, and with the cellulose membrane of vegetable cells." † Fuchs observed a membrane of a certain power of resistance in frogs' red blood-corpuscles after keeping them a few days on the slide without addition of any re-agent, which membrane was particularly obvious when the nucleus made its exit out of the corpuscular mass. ‡ According to A. Bechamp, § and J. Bechamp and Baltus, ‖ the red blood-corpuscles of mammals, birds, and amphibia possess a distinct membrane, which can be thickened by adding a solution of starch to the blood, and then becomes more resistant to the action of water.

It has even been supposed that blood-corpuscles had more than a single membrane; thus Roberts said ¶ his observations had led him "to the belief that the envelope of the vertebrate blood-disk is a duplicate membrane; in other words, that within the outer covering there exists an interior vesicle which incloses the colored contents, and in the ovipara, the nucleus." Böttcher has refuted this notion, ** and it is characterized by Wedl, too, as incorrect; according to Wedl, when the cortical layer becomes swelled and condensed, the double contour which is seen indicates its thickness — but he is "quite certain that whether it be called membrane or not, it is not simply an artificial product." †† Lankester, in his conclusions regarding the vertebrate red blood-corpuscle, says: "Its surface is differentiated somewhat from the underlying material, and forms a pellicle or membrane of great tenuity, not distinguishable with the highest powers (whilst the corpuscle is normal and living), and having no pronounced inner limitation." ‡‡ Ranvier thinks that the double contour — the effect of dilute alcohol — "proves the existence, if not of a membrane, at least of a differentiated cortical layer." §§

Schmidt ‖‖ calls attention to the double contour as being "the only proof

* *Ibid.*, p. 480.

† Compare "Neue Untersuchungen über die rothen Blutkörperchen." Mémoires de l'Academie Impériale des Sciences de St. Petersbourg, vii. Serie, t. xxii. (1876), No. 11, p. 8; and the "Untersuchungen" in Virchow's Archiv, vol. xxxvi. (1866), pp. 357, 383, 387-9, and 404, with Archiv für Mikroskopische Anatomie, vol. xiv. (1877), p. 93, or "On the Minute Structural Relations of the Red Blood-corpuscles" (translated from the preceding in), *Quarterly Journal of Microscopical Science*, October, 1877, p. 392.

‡ "Beitrag zur Kenntniss des Froschblutes," etc., *l. c.*, p. 91.

§ "Recherches sur la Constitution Physique du Globule Sanguin." Compt. Rendus, t. lxxxv. (1878), No. 16, pp. 712-715.

‖ "Sur la structure du Globule Sanguin, et la résistance de son enveloppe à l'action de l'eau." *Ibid.*, No. 17, p. 761.

¶ *L. c.*

** *Op. cit.* Virchow's Archiv, vol. xxxvi. (1866), pp. 392-395.

†† *L. c.*, p. 408.

‡‡ *L. c.*, p. 386.

§§ "De l'Emploi d'Alcool Dilué en Histologie." Archiv de Physique, 1874, pp. 790-793. And again, "Recherches sur les Eléments du Sang." *Id.*, 2 Serie, vol. ii. (1875), pp. 1-15.

‖‖ "The Structure of the Colored Blood-corpuscles of Amphiuma tridactylum, the Frog, and Man." Journal of the Royal Microscopical Society; containing its Transactions and

of the presence of a membrane, whether preëxistent or artificially produced." In fresh blood of amphiuma he has observed colored blood-corpuscles with a greenish border, indicating "the existence of a thin layer at the surface, differing, if not in chemical composition at least in density, from the substance of the disks." He has frequently met with "specimens of blood-corpuscles, on which, by a contraction of the protoplasm representing the greater portion of the whole body, the pellicle in question appears separated from the latter." Once he saw a fragment of a corpuscle on which "the membraneous layer was seen projecting on the torn surface"; and at another time he found "a fresh blood-corpuscle of the amphiuma on which the membraneous layer had apparently burst and retracted, leaving a portion of the underlying material, the protoplasm, exposed." He says: "The changes taking place in these blood-corpuscles, when treated with the solution of the hydrate of chloral, are very interesting and important; as they manifestly show the existence of the membraneous layer of these bodies, such as I have described it. Thus, after the solution has been applied, the protoplasm of the blood-corpuscle, without much or any alteration of form, gradually contracts upon the nucleus. As the result of this contraction, it becomes entirely separated from the membraneous layer, which manifests itself in the form of a delicate double contour. The interspace left between the contracted protoplasm and the double contour representing the membraneous layer is very considerable, as will be seen from the drawings, and, it seems to me, should be sufficient evidence to prove the existence of such a layer to an unbiased mind." In the colored blood-corpuscles of the frog, he has also seen a distinct stratum, or membraneous layer.

"The colored blood-corpuscles of man show a double contour under various circumstances and conditions, indicating the existence, if not of an enveloping membrane, at least of a membraneous layer on its surface." As one proof, Schmidt recommends the experiment of pressing down, by means of the point of a forceps, a small round covering-glass upon a very small drop of fresh human blood placed upon the slide, "with the object of compressing or crushing the blood-corpuscles as far as possible." "Carefully examined with a first-class objective of sufficient amplification, it will be found that they have not run into each other; but that, on the contrary, the outlines of almost every individual may be discerned, however distorted they may be."

Almost all investigators nowadays agree that the colored blood-corpuscles of birds, reptiles, amphibia and fishes have a nucleus; while in those of man and other mammalia, except in developmental forms, a nucleus does not occur. On this difference, Gulliver has founded his division of all vertebrate animals into pyrenæmata and apyrenæmata.* But the existence of a nucleus in living corpuscles of oviparous vertebrata has been denied on the one hand; while, on the other, the opinion has been advanced that the mammalian red corpuscles, as well as those of other vertebrata, are in reality nucleated.

Proceedings, with other Microscopical Intelligence. London, vol. i., No. 2 (May, 1878), pp. 57-78; No. 3 (July, 1878), pp. 67-120.

* "Lectures on the Blood of Vertebrata," *l. c.*; in *Journal of Anatomy and Physiology*, vol. ii.; Proceedings of the Zoölogical Society of February 25, 1862; and Hunterian Oration, 1863, referred to in "Observations on the sizes and shapes of the red corpuscles of the blood of vertebrates, with drawings of them to a uniform scale, and extended and revised tables of measurement." Proceedings of the Zoölogical Society of London, for the year 1875, Part III., p. 479.

Not to cite older authors, I will mention that Funke* asserts that the nucleus of nucleated blood-corpuscles does not exist during life, but is a product of decomposition after death. Likewise Savory, in a paper† read before the London Royal Society, urged that "when living, no distinction of parts can be recognized; and the existence of a nucleus in the red corpuscles of ovipara is due to changes after death, or removal from the vessels"; and furthermore, "the shadowy substance seen in many of the smaller oviparous cells, after they have been mounted for some time, is very like that seen under similar circumstances in some of the corpuscles of mammalia." But Böttcher has reported‡ seeing nucleated blood-corpuscles in the capillaries of living frogs, and more recently Hammond saw a nucleus in the red blood-corpuscles of young trout, varying as to age from a day to three weeks, swimming in a cell full of water;§ and afterward also in those of the tail of frog-embryos and in other animals.‖

Böttcher has by numerous methods and for a long time sought to demonstrate the existence of a nucleus in mammalian red blood-corpuscles. In his first publication¶ he gave a historical sketch of the literature of the subject, and described the effects of chloroform, magenta, tannin, and other re-agents. He also treated corpuscles with serum of other blood; next** he placed them in aqueous humor ("methods which alter the red blood-corpuscles as little and as slowly as possible"); afterward†† he treated them with alcohol and acetic acid, and still more recently‡‡ by means of a concentrated alcoholic solution of corrosive sublimate (methods of "hardening the blood-corpuscles and then extracting the hæmatin from them"). Freer, using reflected instead of transmitted light (by means of Wales' Illuminator), affirmed§§ independently of Böttcher the existence of a nucleus in human blood; and Piper‖‖ seems very desirous to confirm Freer. Brandt, having,¶¶ in the red blood-corpuscles of living sipunculus, occasionally found a nucleus, though usually there is none, thought that perhaps the nuclei are unstable formations which by slight influences are produced or made visible, and by others are destroyed or made invisible; on examining a drop of blood from his finger, on which he had before pricking placed a little fresh chicken albumen, he usually found in

* "Lehrbuch der Physiologie." Leipzig, 1863, vol. i., p. 17.

† "On the Structure of the Red Blood-corpuscle of Oviparous Vertebrata." Proceedings of the Royal Society, vol. xvii., 1868, 1869 (read March 18, 1869). *Monthly Microscopical Journal*, April, 1869, p. 235.

‡ "Untersuchungen über die rothen Blutkörperchen der Wirbelthiere." Virchow's Archiv, vol. xxxvi. (1866), (pp. 342-423), p. 351.

§ "Observations on the Structure of the Red Blood-corpuscles of a Young Trout." *Monthly Microscopical Journal*, June, 1876, pp. 282, 283.

‖ "Observations on the Structure of the Red Blood-corpuscles of Living Pyrenæmatous Vertebrates." *Id.*, September, 1876, p. 147.

¶ The "Untersuchungen" just cited, pp. 359, 363, 367, etc., and 376.

** "Nachträgliche Mittheilung über die Entfärbung rother Blutkörperchen und über den Nachweis von Kernen in denselben." Virchow's Archiv, vol. xxxix. (1868), pp. 427-435.

†† "Neue Untersuchungen über die rothen Blutkörperchen." Mémoires de l'Acad. Imp. des Sci. de St. Petersbourg, vii. Ser., t. xxii., No. 11.

‡‡ "Ueber die feineren Structurverhältnisse der rothen Blutkörperchen." Archiv für Mikrosk. Anatomie, vol. xiv. (1877), pp. 73-93.

§§ "Discovery of a new Anatomical Feature in Human Blood-corpuscles." *Chicago Medical Journal*, May 15, 1868, and April 15, 1869.

‖‖ "Contraction of Blood-corpuscles through the Action of Cold." *New York Medical Journal*, March, 1877, p. 244.

¶¶ "On the Nucleus of Red Blood-corpuscles." Arbeiten der St. Petersb. Gesellsch. d. Naturf., vol. vii. (1876), p. 129. (In the Russian language.)

many red corpuscles what he was inclined to interpret as a central nucleus, in confirmation of the observations of Böttcher.* More recently, Stowell has written a communication to corroborate Böttcher.† And Stricker has expressed the opinion that the nuclei of embryonal colored blood-corpuscles of mammals persist as circular thin disks; he argues that these "disks are so large that the body proper of the corpuscle appears on a surface view as only a narrow zone; and that, therefore, except with high powers, the existence of a nucleus is easily overlooked; and he asserts that, by means of objective No. 15, he has in the blood-corpuscles of man, dog, rabbit, and cat seen the nucleus in both surface and profile views.‡

On the other hand, Schmidt and Schweigger-Seidel, who repeated Böttcher's early methods, using especially chloroform as he had done, failed in finding nuclei, and suspected optical illusion.§ Klebs contradicted Böttcher's statements as to the presence of nuclei in normal mammalian red blood-corpuscles; but described the occurrence of nucleated red corpuscles in blood taken from the corpse of a child who had suffered from leucæmia, agreeing in so far with a like observation of Böttcher.‖ Brunn said ¶ that he had convinced himself that the appearances produced by both of Böttcher's later methods are artificial and optical effects, due to action of the re-agents on the substance of the corpuscles. And, similarly, Eberhardt has come to the conclusion that the remains after the action of different decolorizing re-agents are not nuclei, but stromata deprived of coloring matter; and that a formation unmistakably a nucleus has not yet been demonstrated in adult human and mammalian red blood-corpuscles.** "

Among other questions as to the red blood-corpuscle stated by Beale,†† he asks: "Is it a living corpuscle that distributes vitality to all parts of the organism, or is it simply a chemical compound which readily absorbs oxygen and carbonic acid gases and certain fluids? Is it composed of formative living matter, or does it consist of matter that is inanimate? Does it absorb nutrient matter, grow, divide, and thus give rise to other bodies like itself, or does it consist of passive material destitute of these wonderful powers, and about to be dissolved into substances of simple composition and more nearly related to inorganic matter?"

He answers the first parts of these interrogatories in the negative, and holds that it is "not living, but results from changes occurring in colorless living matter, just as cuticle, or tendon, or cartilage, or the formed material of the liver-cell, results from changes occurring in the germinal matter of each of these cells." He says: "The colorless corpuscles, and those small corpuscles which are gradually undergoing conversion into red corpuscles,

* "Bemerkungen über die Kerne der rothen Blutkörperchen." Archiv für Mikrosk. Anatomie, xiii. 2 (1876), p. 392.

† "Structure of Blood-corpuscles." *American Journal of Microscopy and Popular Science*, New York, June, 1878, p. 140.

‡ "Vorlesungen über allgemeine und experimentelle Pathologie." II. Abtheilung. Wien, 1878, p. 438.

§ "Einige Bemerkungen über die rothen Blutkörperchen." Bericht der Königl. Sächsischen Gesellschaft der Wissenschaften, 1867, p. 190.

‖ "Ueber die Kerne und Scheinkerne der rothen Blutkörperchen der Säugethiere." Virchow's Archiv, vol. xxxviii. (1867), p. 200.

¶ "Ueber die den rothen Blutkörperchen der Säugethiere zugeschriebenen Kerne." Archiv für Mikroskopische Anatomie, vol. xiv., Heft 3 (1877), pp. 333–342.

** "Ueber die Kerne der rothen Blutkörperchen der Säugethiere und des Menschen." Inaugural-Dissertation der medizinischen Fakultät zu Königsberg. April, 1877, p. 30.

†† "Observations upon the Nature of the Red Blood-corpuscle"; *l. c.*, p. 32.

are living, but the old red corpuscles consist of inanimate matter. They are no more living than the cuticle or the hard, horny substance of nail or hair is living." * He therefore denied the contractility and amœboid movement of colored blood-corpuscles.

Klebs was the first who accorded them life and contractility. † He did this because, on preventing evaporation and raising the temperature of blood, he noticed, aside from motion of the corpuscles, the protrusion and retraction of knobs, and the formation and disappearance of scallops. But though the correctness of his observation was not doubted, his inferences were strenuously contradicted by Rollett and others. ‡ Lankester observed "amœboid figures" when colored blood-corpuscles had been subjected to the action of dilute ammonia and acetic acid, of which he says: § "The behavior of these corpuscles under alternate weak ammoniacal and acid vapors furnished a very curious parallel to the movements of amœboid protoplasm, and a careful consideration of the phenomena may throw some light on the nature of protoplasmic contractility." Böttcher admits the possibility of vital contractility, but thinks it cannot be compared to that of colorless blood-corpuscles. ‖ Brücke,¶ also, admits cautiously this possibility. Preyer ** uses many qualifying expressions, such as "only in part," "under certain circumstances," "in some degree," "temporarily," "at certain times." He observed active form-changes of red corpuscles in extravasated amphibian blood, examined in the moist chamber, which led him to the conclusion that "the substance of these corpuscles consists of dissolved coloring matter and a colorless material (protoplasma) which, both when still in connection with the coloring matter and when free from this, shows under certain circumstances phenomena of contractility similar to those observed in many lower organisms." He adds: "As a rule it evinces no contractility, and constitutes, as a modified protoplasm, the stroma of amphibian blood-corpuscles." †† Max Schultze, who denied the contractility of red blood-corpuscles of man and mammals (although when subjected to a very high temperature—fifty to fifty-two degrees C., nearly enough to kill them—he saw protrusions and detachments of portions), admitted that the red blood-corpuscles of very young chicken-embryos are contractile. ‡‡ Friedreich §§ observed in an enfeebled anæmic patient polymorphous red blood-corpuscles, with active though very slow form-changes, which he could not but interpret as the result of contractility. In the *post mortem* blood of a woman who had been leucæmic he saw similar polymorphous corpuscles; and in a case of albuminous urine he repeatedly observed colored blood-corpuscles from which minute portions became constricted and separated, as well as those which

* *Ibidem*, p. 43.

† Centralblatt für medizinische Wissensch., 1863, No. 514, p. 851.

‡ For the views of Rollett, Max Schultze, Kühne, etc., see "Stricker's Handbuch," *cit.*, Leipzig (1869) edition, p. 287; American reprint (1872), p. 286.

§ *Op. c.*, p. 378.

‖ Archiv für Mikr. Anat., vol. xiv. *cit.* p. 91; translated in *Quarterly Journal of Microscopical Science*, Oct., 1877, p. 391.

¶ *L. c.*

** *Op. c.*, p. 417 *et seq.*

†† *Ibid.*, p. 440.

‡‡ Verhandlungen der Niederrheinischen Gesellschaft für Natur und Heilkunde in Bonn, am 8 Juni, 1864; Berliner Klinische Wochenschrift, 1864, No. 36, p. 358.

§§ "Ein Beitrag zur Lebensgeschichte der rothen Blutkörperchen." Virchow's Archiv, vol. 41 (1867), p. 395.

exhibited amœboid protrusion and retraction of short blunt projections, whereby a slow locomotion of the corpuscle was accomplished. He assumed that the contractility which the colorless corpuscles possess in so high a degree is preserved in undiminished strength in the red corpuscles in certain pathological cases. According to Charlton Bastian,* red blood-corpuscles leave under certain circumstances the vessels by virtue of active amœboid movements; and he thinks it would be well if "the attention of future observers should be directed to these peculiarities, and to the particulars above mentioned, in order to determine more certainly than has yet been done how far amœboid movements and contractions do take place in the much-examined and much-written-about red blood-corpuscles."

Lieberkühn observed in the red corpuscles of salamandra and pike's blood active protrusion and retraction of bead-like processes. He also saw movements of granules or small molecules in the interior of the red blood-corpuscles of living frog embryos.†

Faber,‡ in addition to his own observations of contractility and spontaneous locomotion of colored blood-corpuscles in albuminous urine,—phenomena which continued to be manifested for a longer time in colored than in colorless corpuscles,—has given a rather complete account of the literature of these phenomena, including the reports of diapedesis observed by Virchow, Stricker, Cohnheim, Prussak, and Hering. The observations of amœboid movements by Bastian (just cited), Owsjannikow,§ Winkler,‖ and Brandt¶ seem to have escaped him; Arnold's experiments concerning diapedesis,** and Belfield's observation of emigration of certain small-sized red corpuscles of the frog,†† were published more recently. Since the publication of Faber's article, furthermore, Rommelaere has described amœboid movements of colored blood-corpuscles;‡‡ Brandt §§ has spoken of the peculiar forms of the red blood-corpuscles of sipunculus and phascolosoma referable to amœboid movements, and of the fact that occasionally in the temperature of an ordinarily warmed room considerable movements are accomplished; and Schmidt has observed spontaneous motion (expansion and contraction) in a fresh colored blood-corpuscle of amphiuma in one instance,‖‖ and in those of man in a number of instances. He reports that he had witnessed the phenomenon in the colored blood-corpuscles of man as early as the summer of 1871. He says: "In examining a specimen of human blood, and whilst my attention was directed to the colored corpuscles as they were carried along by a moderate current of the liquor sanguinis under the covering-glass, I noticed on some of

* "Passage of the Red Blood-corpuscles through the Walls of the Capillaries in Mechanical Congestion." *British Medical Journal*, May 2, 1868, pp. 425, 426.

† "Ueber Bewegungserscheinungen der Zellen." Schriften der Gesellschaft zur Beförderung der gesammten Naturwissenschaften zu Marburg, vol. ix. (1870), p. 335.

‡ "Ueber die rothen Blutkörperchen." Archiv der Heilkunde, xiv. (1873), pp. 481-511.

§ *Op. cit.*, p. 563.

‖ "Textur, Structur, und Zellleben in den Adnexen des Menschlichen Eies," Jena, 1870, p. 33.

¶ "Anatomisch-hist. Untersuchungen über d. Sipunculus nudus, L." Memoires de l'Académie Imperiale des Sciences de St. Petersbourg, vii. Serie, t. xvi., No. 8.

** *Loc. cit.*

†† "Emigration in Passive Hyperæmia." *American Quarterly Microscopical Journal*, October, 1878, p. 39.

‡‡ "De la Déformation des Globules Rouges du Sang." Bruxelles, 1874, p. 47.

§§ In a foot-note to his "Bemerkungen über die Kerne der rothen Blutkörperchen," *l. c.*, pp. 391, 392.

‖‖ *Op. cit.*, p. 67.

them the projection and immediate withdrawal of minute, conical, thorn-like processes, whenever one blood-corpuscle came into the vicinity of another, without, however, actual contact. It seemed almost as if one corpuscle were attracting or drawing out the thorn-like process from the surface of the other. In other instances, however, I observed the shooting forth and quick withdrawal of these processes from the margins of corpuscles not in close vicinity to others. As these processes appeared at the marginal surfaces of the blood-corpuscles, before the latter had come in contact with other of their fellows, I naturally regarded the phenomenon as one of spontaneous motion, manifested by the colored blood-corpuscle. But as in most instances the phenomenon was observed in corpuscles passing near each other, I was inclined to attribute it to a certain power of mutual attraction, residing under certain conditions in the colored blood-corpuscles. Having taken the precaution of slightly warming the glass slide before putting the blood, quickly taken from the vessels of the skin of a vigorous young man, upon it, and the temperature of the surrounding air being ninety-six degrees F., or even more, at the time, I also considered a certain amount of heat, at least ninety-eight degrees F., as essential to the manifestation of the phenomenon. This view, however, proved to be erroneous, as I shall show directly. Although I have witnessed this phenomenon on blood-corpuscles when in a state of rest, it nevertheless is more frequently observed on blood-corpuscles in motion, as when they are carried along by a current arising in the specimen under the covering-glass, and resembling in character the current in the capillary vessels. With this view, the drop of blood should be thinly spread upon the glass slide, and quickly covered with the thin plate of glass. While the blood-corpuscle is projecting the thorn-like process, its body elongates, resembling a unipolar cell, but with the withdrawal of the process generally assumes its original round form; bipolar or lemon-shaped corpuscles are also very frequently met with in specimens of human blood. The same process is also observed when the margins of two corpuscles actually touch each other very slightly, and then slowly separate again. While separating, the thorn-like processes will be drawn out at the exact place of contact, and either remain permanent or disappear again after the separation has taken place.

"That the normal heat of the human blood is not essential to the manifestation of spontaneous motion in the colored corpuscles, I discovered during the past winter, while repeating my examinations of the structure of these bodies. I then witnessed the phenomenon above described, without having warmed the glass slide and covering-glass, and at the temperature of a moderately warmed room. However, I observed a colored corpuscle of a constricted form, similar to a figure of eight, slowly expanding, and finally resuming its original round form.

"From this we may conclude that the colored blood-corpuscle of man possesses not only a certain inherent power of contracting its body, but also of resuming its original form by a subsequent expansion, a characteristic property of the living protoplasm enabling the colored corpuscle to manifest spontaneous motions, though not to so great an extent as is seen in the colorless." *

In his "General Conclusions and Summary," Lankester † says that the viscid mass constituting the red blood-corpuscles of the vertebrata "consists

* *Op. cit.*, pp. 113-115.

† *Op. cit.*, p. 386.

of (or rather *yields*, since the state of combination of the components is not known) a variety of albuminoid and other bodies, the most easily separable of which is hæmoglobin; secondly, the matter which segregates to form Robert's macula; and thirdly, a residuary stroma apparently homogeneous in the mammalia (excepting so far as the outer surface or pellicle may be of a different chemical nature), but containing in the other vertebrata a sharply definable nucleus; this nucleus being already differentiated but not sharply delineated during life, and consisting of (or separable into) at least two components, one (paraglobulin) precipitable by CO_2, and removable by the action of weak NH_3; the other pellucid and not granulated by acids."

A residuary stroma, such as Lankester here speaks of, seems to have been first recognized by Nasse, who said* that the red blood-corpuscle "consists of a basis tissue, insoluble in water, which is penetrated by a red substance, probably dissolved, or at least in water easily soluble (the red coloring matter of the blood), and some water, and within which there is an aggregation of solid granules not connected with the coloring matter." Rollett,† also, assumed that a stroma or matrix enters into the structure of the colored elastic extensible substance of the red blood-corpuscle, to which the form and the peculiar physical properties of the corpuscle are due. This stroma is, however, according to Böttcher, an artificial product, "nothing more than a residue of the colorless part of the red blood-corpuscles, varying much in form and extent, which remains after the dissolution of the original structural relations."‡ Brücke considered the most probable interpretation of the forms of colored blood-corpuscles, based on their appearances after the addition of boracic acid, to be the existence of a porous mass of motionless, very soft, colorless, hyaline substance, which he calls œcoid, in the interspaces of which is imbedded the living body of the corpuscle; which body he calls zooid, and which consists of the nucleus (where that exists) and all the remaining part of the corpuscle containing the hæmoglobin.§ But Rollett insisted that the forms on which Brücke based this interpretation are products of decomposition.‖ Stricker agrees with Brücke as to the existence of the œcoid, but separates, in oviparous corpuscles, the remaining portion into nucleus and body.¶ Of the three views thus presented, Lankester gives, after Stricker, the following tabular statement:**

Red blood-corpuscles of ovipara, divisible into	Stroma. Coloring matter.	According to Rollett.
	Œcoid = outer part of stroma. Zooid = rest of stroma plus hæmoglobin.	According to Brücke.
	Membrane = œcoid. Body = zooid minus nucleus. Nucleus = zooid minus body.	According to Stricker.

* "Blut." R. Wagner's "Handwörterbuch der Physiologie." Braunschweig, 1842, vol. i., p. 89.

† "Versuche und Beobachtungen am Blute." Moleschott's Untersuchungen, ix.; also Sitzungsberichte der Wiener Akademie, vol. xlvi., Div. 2 (1862), pp. 65-98; and Stricker's "Handbuch," *cit.* Leipzig edition, 1869, p. 295; American, p. 284.

‡ *Op. cit.*, Archiv für Mikroskopische Anatomie, p. 90, translated in *Quarterly Journal of Microscopical Science*, October, 1877, p. 390.

§ "Ueber den Bau der rothen Blutkörper"; Sitzungsberichte der Wiener Akademie, vol. lvi., Div. 2 (1867), p. 79.

‖ "Ueber Zersetzungsbilder der rothen Blutkörperchen"; Untersuchungen aus dem Institute der Physiologie und Histologie in Graz. Leipzig, 1870, p. 1.

¶ "Mikrochemische Untersuchungen der rothen Blutkörperchen"; Archiv für die gesammte Physiologie des Menschen und der Thiere (Pflüger's), vol. i. (1868), p. 592.

** *Op. cit.* in a foot-note to p. 374.

If it had not been for the deserved eminence in other respects of the three investigators, Rollett, Brücke, and Stricker, these notions of the structure of colored blood-corpuscles would probably never have attracted any attention.

Laptschinsky * considered colored corpuscles to consist of two kinds of substance,—viz., one which appears smooth, soft, extensible, assumes mostly a roundish form, and altogether possesses some if not all of the properties of the so-called stroma; the second, visible under the microscope only when through the action of different re-agents it is precipitated, or swelled, or both. It is this second substance which, on staining, takes up the coloring matters, and, by separating in the interior of the corpuscle from the first substance, or protruding from it, gives rise to the various shapes observed. At present it cannot be determined in what relation these two substances stand to each other previous to the precipitation of the stainable portion. The separating the blood-corpuscles into the two substances mentioned is brought about by various external influences.

In amphibian, *i. e.*, frogs' and salamanders', red blood-corpuscles, Hensen, Böttcher, Kollmann, and Fuchs have seen a net-work; and although they have failed to interpret it correctly—as is evident from the context of their descriptions—I beg to call special attention to their observations.

Hensen ascribed to the corpuscle the possession of protoplasm accumulated at the nucleus and at the inner surface of the membrane; the two being connected by delicate radiating filaments, in the spaces between which the colored cell-liquid lies.†

Böttcher, from his observations, "inferred that around the nucleus of the amphibian blood-corpuscles a mass of protoplasm is collected, which radiates in the form of filaments into the homogeneous red substance. . . . The protoplasm appears sometimes collected uniformly round the nucleus, at other times it is accumulated more to one side of it. It is either provided with only a few processes, or is arranged round the nucleus in the shape of an elegant star, whose points extend to the margin of the corpuscle, or else it forms round the nucleus a peculiar lobed figure. Very often it appears beset on one or all sides with fine, hair-like processes. Then, again, it may represent a sort of net-work, which either appears separated from the less darkly colored cortical layer and more contracted, or else it throws out into the cortex innumerable very fine radiating filaments, so that its processes approach the extreme periphery of the blood-corpuscles. In this case, therefore, the whole blood-corpuscle is permeated by a net-work of fine filaments." ‡

According to Kollmann, the membrane incloses a net-work of delicate slightly granular albumen threads. These in their totality constitute the stroma, and in the small spaces between the threads of the stroma lies the hæmoglobin. The soft, elastic albumen threads are stretched between membrane and nucleus. Only by a certain degree of their tension is the characteristic form of the blood-corpuscle possible. The hæmoglobin in the meshes counteracts excessive shortening of the threads. §

Fuchs expresses himself similarly as to the net-work of fibers emanating from the nucleus, and going to the periphery of the frog's red blood-corpuscle.

* "Ueber das Verhalten der rothen Blutkörperchen," *loc. cit.*, pp. 173, 174.

† "Untersuchungen," *l. c.*, p. 261.

‡ "On the Minute Structural Relations of the Red Blood-corpuscles." *Quarterly Journal of Microscopical Science*, Oct., 1877, pp. 388–390.

§ "Bau der rothen Blutkörperchen," *l. c.*, p. 482.

He adds that the net-work gives the corpuscle its shape, and fixates the nucleus in the center. Death of the corpuscle produces first coagulation, afterward liquefaction of the fibers of the net-work. Whenever the fibers are coagulated they are shortened, and produce indentations at the surface by drawing upon the points where they are attached; when the shortening proceeds too far, the fibers are torn off from the membrane, and in both cases of shortening there are places at the surface which look protruded. Liquefaction of the fibers is assumed when the corpuscle has a vesicular appearance, when it seems to contain a semi-fluid mass in which the nucleus may take any position, and from which it sometimes exudes, proving in exuding the existence of a membrane as already described.*

Schmidt seems to have seen something like an arrangement of filaments, but, if so, has misinterpreted it entirely. He has reported observing in blood of amphiuma treated first with water under the microscope, and then with a very weak solution of chromic acid (strength not ascertained), "a series of fine lines, radiating from the periphery of the nucleus through the protoplasm to the inner surface of the membraneous layer of the blood-corpuscle." He remarks: "Now this picture would almost seem to corroborate the theory of Hensen, as well as that of Kollmann; the fine double lines representing the filaments, which they suppose to radiate from the nucleus to the enveloping membrane. But this is not the case; for a closer examination reveals that these lines represent nothing but fissures in the protoplasm, which appears to have assumed some form of crystallization. This becomes more evident by observing some of these fissures deviating from their course, and giving rise to subordinate branches."† He has also reported a somewhat analogous appearance in the colored blood-corpuscles of the frog, both fresh and treated with the same re-agents. This he explained by contraction of the interior mass. He says: "The protoplasm in such a case retracts upon the nucleus, which it completely surrounds, while the membraneous layer appears isolated, manifesting itself by a double contour. And again, if the same process should take place without entirely separating the protoplasm from the membraneous layer, but leaving at certain small points a union between the two parts, the result must be the production of a number of filamentary processes, arising from the main bulk of the protoplasm, and passing to those points of the membraneous layer."‡

Kneuttinger considered the two surfaces of the biconcave disk of blood-corpuscles to be connected at the place of the depression by protoplasma threads; if these tear, the biscuit form changes to a sphere. §

According to Krause, the red blood-corpuscle consists of: 1. A colorless stroma formed by a solid albuminous matter arranged into radial fibers, and 2. Hæmoglobin, which is a colored fluid albuminous matter lying in the interspaces of these fibers. ‖

Lieberkühn has found that the free nuclei of red blood-corpuscles of salamandra and tritons (the blood having been kept for some time in colored glass tubes) consists of two substances, of which one forms the

* *Op. cit.*, p. 95.
† *Op. cit.*, p. 72.
‡ *Ibid.*, p. 106.
§ "Zur Histologie des Blutes." Würzburg, 1865, p. 22.
‖ "Allgemeine und Mikroskopische Anatomie," p. 325-334.

envelope and septa or threads passing more or less regularly through the interior, the other being contained between these septa.*

In the nuclei of colored blood-corpuscles, Bütschli, W. Flemming, and Klein have reported the existence of a net-work, viz.:

In the nuclei of red blood-corpuscles of frog and newt, Bütschli observed fibrils, with granular thickenings, traversing the nucleus and passing to and connecting with its envelope.†

Flemming saw a very delicate and dense net-work of fibers pervading the interior of the nucleus, and attached to the nuclear membrane in many so-called cellular elements of the bladder of curarized salamandra maculata. He inferred that the net-work is present also in the nuclei of the red blood-corpuscles, though he did not see it there.‡

Speaking of some capillary blood-vessels of a newt, Klein said: "Some such capillaries contained blood-corpuscles, and the nuclei of these showed a very distinct net-work." § Also: "The examination of the nuclei of fresh epithelium of frog, toad, or newt, the nuclei of fresh colored corpuscles of these animals, especially of toad, with a Zeiss's F lens, or a Hartnack's immersion, No. 10, reveals fibrils in the nucleus, and also shows that the 'granules' are due to the twisted or bent condition of them."

III.

The method employed in my investigation, viz.: treatment of fresh blood with solution of bichromate of potash, and examination with high magnifying power, has revealed certain appearances as the structural arrangements of colored blood-corpuscles. Do these arrangements exist in the living corpuscle, or are they artificial productions of the re-agent?

Dilute solutions of bichromate of potash and Müller's fluid are known as the best preserving media for the most delicate animal structures: nervous tissue, the eye, embryos, etc., are kept in them unchanged for any length of time. In the fecundated chicken-egg of only twenty hours, placed in such a solution, the heart, but just formed, has been known to continue for a time to beat. Rollett has investigated the influence of bichromate of potash on protoplasm, and found that no alterations were produced. In my series of observations, the weakest solutions (ten per cent. saturated solution or less) produced no paling of the colored corpuscles; while, on increasing the strength up to a

* *Loc. cit.*

† "Studien über die ersten Entwickelungsvorgänge der Eizelle, die Zelltheilung und die Conjugation der Infusorien." Abhandlungen der Senckenbergischen Naturforschenden Gesellschaft, vol. x., Heft 3, 4 (1876), p. 260.

‡ "Beobachtungen über die Beschaffenheit des Zellkernes." Archiv für Mikroskopische Anatomie, vol. xiii. (1876), p. 693 *et. seq.*

§ "Observations on the Structure of Cells and Nuclei." *Quarterly Journal of Microscopical Science*, July, 1878, p. 337.

‖ *Ibid.*, p. 332.

certain point, paling occurred in an increasing degree, and a morphological structure became visible at the same time that the manifestations of life (contraction and amœboid movement) continued. From this we certainly may infer that the re-agent has not altered, at all events not seriously impaired, the living matter; and when we find that the structural arrangements thus revealed are the same as those demonstrable without re-agents in other living matter, the inference that they were preëxisting, and not artificially produced by the re-agent, becomes a certainty.

The knowledge of the structure of colored blood-corpuscles will not enable us to solve all the problems regarding their nature; but some questions are answered pretty conclusively by my investigation.

The colored blood-corpuscle is not a cell in any proper sense of that word, but, like the colorless corpuscle, is an unattached portion of the living matter (bioplasson) of the body. Broadly speaking, the essential difference between the two kinds of corpuscles is the presence of hæmoglobin, using this term to designate the substance or substances—no doubt chemically very complicated—constituting the coloring matter under all the varying physiological circumstances.

In size, human colored blood-corpuscles vary so much, that claims to be able to distinguish them by their size from certain other mammalian colored blood-corpuscles are inadmissible.

The colored blood-corpuscle has no separate investing membrane; nevertheless, the outer portion, essentially like the inner substance forming the net-work, may be considered to be differentiated from the latter, especially at the periphery of the disk, where it constitutes an encircling band of uniform thickness, or occasionally of a wreath-of-beads appearance. In the colored blood-corpuscles of the lower classes of vertebrate animals there is usually a nucleus to be seen, which is not the case, as a rule, in those of man, and other mammalians; but there is in the interior of these an accumulation of matter occasionally met with, which may be interpreted as a nucleus.

In the communication to the Vienna Academy, in 1873, Heitzmann demonstrated the existence of a net-work in amœbæ, blood-corpuscles of astacus and of triton, human colorless blood-corpuscles and colostrum corpuscles; and, from direct observation of the changes in the reticulum during the contraction of the living body, announced that the substance constituting the net-work is itself the living matter or bioplasson—*i. e.*, "the

nucleolus, the nucleus, the granules with their threads, are the living contractile matter proper." Aside from some conditions which do not here concern us, he described and illustrated three states of the net-work—viz., that of rest, that of contraction, and that of extension.

A fourth state of the living matter is assumed (hypothetically) by the same investigator, to account for the formation of a flat layer of living matter, such as forms the walls of a vacuole, the membrane of a nucleus, or the outer layer of the whole bioplasson mass.

Heitzmann believes that each of these states may at any time change into the other—*i. e.*, that the net-work may from the condition of rest be transformed into that of contraction, or of extension, or of flattening, and from each of these into either of the others. At all events, there may arise in the bioplasson body a vacuole having a continuous thin wall, and containing lifeless fluid and detached particles of the living matter. Or, a bioplasson mass may take into its interior foreign bodies by forming around them a *cul-de-sac*, which then opens toward the center and closes at the periphery, and the net-work, rent during the process, reëstablishes itself. Again, a bioplasson body, which by flap or knob protrusion and separation has lost a portion of its substance, as well as the portion detached, may become rounded off—the rupture at the place of detachment healing in each case without loss of life. And further, two bioplasson bodies may coalesce, and a portion of the periphery of each be transformed into the uniting net-work.

By adopting these views, and applying them to the living matter of colored blood-corpuscles, we may explain the changes which they have been observed to be subject to. What are the changes that occur on the addition of a 40 per cent. saturated solution of bichromate of potash? I have described indentations and protrusions which either persist or are leveled again; protrusion of knobs, either pedunculated or sessile, which sometimes are so numerous that they surround the body of the corpuscle like a wreath; decrease of the size of the main body by detachment of knobs; appearance of net-work structure, most marked in the corpuscles which have not lost much of their substance; vacuolation of corpuscles, and transformation of many of the portions detached into vacuoled globules which increase in size; finally, change into faint, almost structureless disks, the so-called "ghosts."

The regular rosette, stellated, and thorn-apple shapes are caused by a uniform concentric contraction of the living matter; the fluid in the interior, being pressed toward the outer layer between the points of attachment of the threads, will produce a bulging out at the periphery. Irregular contractions of the living matter will give rise to irregular flaps at the periphery.

An indentation is due to locally limited contraction of the net-work in the interior of the corpuscle. Contraction of the living matter at one part of the periphery will bring about a protrusion of a flap at another, the flap being bounded by the outer layer of the corpuscle.

Segmental contraction of the net-work will produce a rupture of the outer layer of the corpuscle, with projection of a pedunculated granule or knob, formerly a part of the interior net-work. Continued contraction will be followed by the rupture of the pedicle and the production of either so-called detritus or small granules, or when the protruded knob is larger, or has become swelled, of a pale-grayish disk.*

Lastly, a large amount of the net-work having been separated from the parent body, the latter becomes transformed into a pale disk, in which no traces of a net-work, or but very indistinct ones, are visible, a so-called ghost.

At every stage of the protrusion of either flaps or pedunculated knobs or granules, the living matter may be overtaken by death, and the contraction become fixed by cadaveric rigidity. It may perhaps be worth while to notice that irregular contractions have a somewhat greater tendency to such permanency than regular ones; these more frequently yielding, by relaxation of the net-work, or reëstablishment of the state of rest, at impending death. But in the blood-corpuscles kept for over two years in bichromate of potash, all the described forms can be observed just as well as in freshly made specimens.

* The peculiar corpuscles believed to be characteristic of syphilis by Lostorfer, and proved by Stricker to be present in the blood of individuals broken down by that and various other diseases, are nothing but such disks—*i. e.*, portions of the colored blood-corpuscles protruded from the interior, detached and more or less swelled. As persons in low states of health have a relatively small amount of living matter in the same bulk, or, in other words, only a delicate net-work within the bioplasson body or plastid (the so-called "cell"), such a net-work suspended in a relatively large amount of fluid can much more easily contract and bring about a rupture of the outer layer, than in the case of healthy persons, within whose plastids there is relatively less room for contraction to take place.

The reason why the corpuscles of the smallest size do not change in the solution of bichromate of potash of medium concentration, is, perhaps, that, being compact masses of living matter in which the hæmoglobin is not as yet accumulated within meshes, the solution does not reach and cannot extract the hæmoglobin. These small globules are probably intermediate stages of development of colored blood-corpuscles, or the so-called hæmatoblasts of Heitzmann * and of Hayem.†

The Origin of Colored Blood-corpuscles. In 1872, ‡ at a time when I was ignorant of the structure and differences of bioplasson, according to its development, and consequently adhered to the cell-theory, I made the following statements:

Formation of Blood from Cartilage. In a horizontal section of the condyle of a femur of a recently killed dog, several weeks old, we recognize, upon adding a drop of a one-half per cent. solution of chloride of sodium, with moderate powers of the microscope, two kinds of cartilage-corpuscles,—*first:* large, pale granular, distinctly nucleated cartilage-corpuscles; and *second:* smaller shining, yellowish, indistinctly granular corpuscles, devoid of nuclei. There are transitions between these two kinds. Still more marked is the difference in sagittal (antero-posterior) sections of the cartilaginous epiphysis of the same dog. Near the articular surface, the corpuscles, closely arranged, look uniform; but the nearer we come to the diaphysis, the more marked is the difference between the pale and the yellow, shining corpuscles. The glistening substance is often found in a crescent shape around the pale granular, or it occupies the center of the latter in the shape of a globular or irregularly angular body.

Close to the border of the calcified basis-substance, the difference between the two kinds of cartilage-corpuscles is very marked. In a cavity of the basis-substance we often find the shining, coarsely granular substance characterized by thorny offshoots, and surrounded by a pale, granular zone, between which and the basis-substance there is an apparently structureless rim. Solution of chloride of gold renders the finely granular bodies pale violet, whereas the coarsely granular ones assume a dark violet color, retaining their luster.

* "Studien am Knochen und Knorpel." Med. Jahrbücher, 1872.

† "Sur l'Évolution des Globules rouges dans le Sang des Vertébrés." Compt. rend. Acad. des Sci., Nov. 12, 1877; *Idem.* Soc. de Biologie, Nov. 24, 1877. "Sur l'Évolution des Globules rouges dans le Sang des Animaux supérieurs." Compt. rend. Acad. des Sci., Dec. 31, 1877.

‡ "Studien am Knochen und Knorpel." Medic. Jahrbücher, Wien, 1872.

he older an animal (dog, cat, or rabbit) we examine, the ıer we find its articular cartilage, and the less of shining, ıely granular corpuscles; in the cartilage of a very old such corpuscles were entirely wanting—only pale granular eated were present.

In the calcified border of the articular cartilage of a young it, I found large spaces in the narrow calcified basis-substance, h were partly filled with a colorless, finely granular protom, and their centers exhibited the glistening substance. In large spaces below these, groups of bright lumps of differ-

. 27.—CONDYLE OF FEMUR OF A YOUNG RABBIT, AT THE BORDER OF CALCIFICATION OF THE DIAPHYSEAL CARTILAGE. SAGITTAL SECTION. [PUBLISHED IN 1872.]

CC, cartilage-corpuscles, filling the spaces of the calcified basis-substance, CA; changing the level into hæmatoblasts, L, and below this level into medullary corpuscles, P. The bles in the middle of the medullary spaces are forming blood-vessels. Magnified 800 meters.

them the projection and immediate withdrawal of minute, conical, thorn-like processes, whenever one blood-corpuscle came into the vicinity of another, without, however, actual contact. It seemed almost as if one corpuscle were attracting or drawing out the thorn-like process from the surface of the other. In other instances, however, I observed the shooting forth and quick withdrawal of these processes from the margins of corpuscles not in close vicinity to others. As these processes appeared at the marginal surfaces of the blood-corpuscles, before the latter had come in contact with other of their fellows, I naturally regarded the phenomenon as one of spontaneous motion, manifested by the colored blood-corpuscle. But as in most instances the phenomenon was observed in corpuscles passing near each other, I was inclined to attribute it to a certain power of mutual attraction, residing under certain conditions in the colored blood-corpuscles. Having taken the precaution of slightly warming the glass slide before putting the blood, quickly taken from the vessels of the skin of a vigorous young man, upon it, and the temperature of the surrounding air being ninety-six degrees F., or even more, at the time, I also considered a certain amount of heat, at least ninety-eight degrees F., as essential to the manifestation of the phenomenon. This view, however, proved to be erroneous, as I shall show directly. Although I have witnessed this phenomenon on blood-corpuscles when in a state of rest, it nevertheless is more frequently observed on blood-corpuscles in motion, as when they are carried along by a current arising in the specimen under the covering-glass, and resembling in character the current in the capillary vessels. With this view, the drop of blood should be thinly spread upon the glass slide, and quickly covered with the thin plate of glass. While the blood-corpuscle is projecting the thorn-like process, its body elongates, resembling a unipolar cell, but with the withdrawal of the process generally assumes its original round form; bipolar or lemon-shaped corpuscles are also very frequently met with in specimens of human blood. The same process is also observed when the margins of two corpuscles actually touch each other very slightly, and then slowly separate again. While separating, the thorn-like processes will be drawn out at the exact place of contact, and either remain permanent or disappear again after the separation has taken place.

"That the normal heat of the human blood is not essential to the manifestation of spontaneous motion in the colored corpuscles, I discovered during the past winter, while repeating my examinations of the structure of these bodies. I then witnessed the phenomenon above described, without having warmed the glass slide and covering-glass, and at the temperature of a moderately warmed room. However, I observed a colored corpuscle of a constricted form, similar to a figure of eight, slowly expanding, and finally resuming its original round form.

"From this we may conclude that the colored blood-corpuscle of man possesses not only a certain inherent power of contracting its body, but also of resuming its original form by a subsequent expansion, a characteristic property of the living protoplasm enabling the colored corpuscle to manifest spontaneous motions, though not to so great an extent as is seen in the colorless." *

In his "General Conclusions and Summary," Lankester † says that the viscid mass constituting the red blood-corpuscles of the vertebrata "consists

* *Op. cit.*, pp. 113-115.

† *Op. cit.*, p. 386.

do not, either inside or outside of the vessels, which themselves are not fully developed, exhibit the features of perfect red blood-corpuscles, but show the most convincing transitions toward such, we are certainly justified in saying that they are stages of development of colorless protoplasm into colored corpuscles. We may designate such formations as hæmatoblasts.

I thus saw formations also met with by W. H. Carmalt and S. Stricker* in the inflamed cornea of the frog and rabbit, and

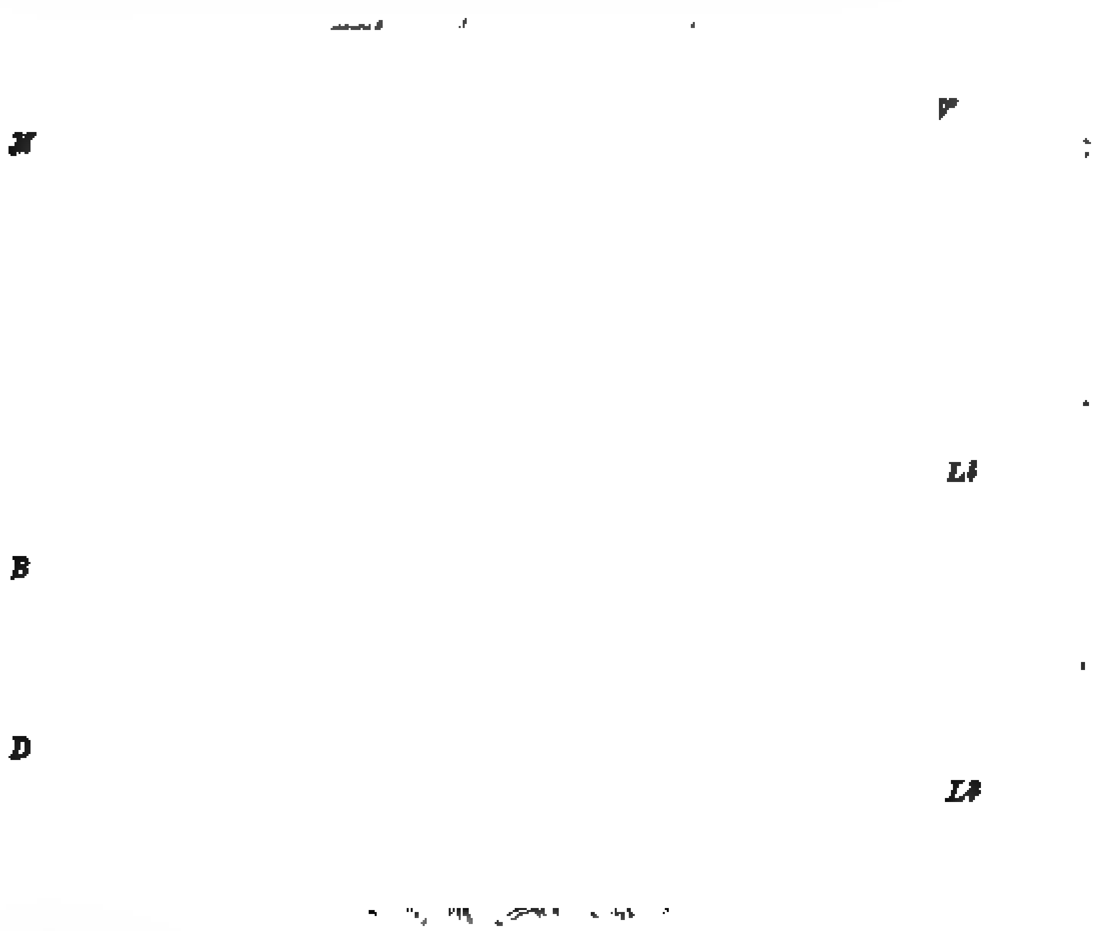

FIG. 29.—HÆMATOBLASTS IN BONE-CORPUSCLES OF A DOG'S TIBIA, PURPOSELY INJURED WITH A RED-HOT IRON. EIGHTH DAY OF INFLAMMATION. [PUBLISHED IN 1872.]

Bright homogeneous lumps, L^1 and L^2, contain a few vacuoles, *V*, or numerous vacuoles, *D*. The shining substance borders the bone-corpuscle at *M*; a fully formed red blood-corpuscle at *B*. Magnified 800 diameters.

could corroborate the statement of C. Rokitansky † that in "mother-cells," when they ramify in order to produce a capillary ystem of vessels, blood originates.

In 1873 (page 46), I claimed all the formations described to e living matter at an early, juvenile stage, from which, in turn, y vacuolation and reticulation, protoplasmic bodies may arise.

* Medic. Jahrbücher. Wien, 1871.
† Handbuch der allg. patholog. Anatomie. Wien, 1846.

Lumps of living matter, however, separated from the neighboring formations and suspended in plasma, in blood-vessels, I still considered as blood-formers—hæmatoblasts.

The idea prevailed at that time that red blood-corpuscles originate from nucleated, colorless corpuscles, although no other support was found for this idea except that in the embryo there are numerous nucleated corpuscles in the blood-vessels. All attempts to transform colorless into colored blood-corpuscles outside the body, by their exposure to oxygen gas, proved to be failures. I have shown that whenever one tissue is transformed into another,—f. i., cartilage into bone, and also in an inflamed tissue, f. i., that of bone,—colored blood-corpuscles grow from granules of living matter in a way entirely different from that supposed by other histologists.

E. Neumann* first drew attention to a difference in the shape of the corpuscles of the medulla of bone. In the liquid pressed out of this tissue he found colorless, granular lymph-corpuscles and yellow corpuscles, characterized by a homogeneous appearance, and a size only a little exceeding that of red blood-corpuscles. He met with colored cells in the medulla of bone, in numbers the greater the younger the individual, and interpreted these to be stages of transition to red blood-corpuscles. He also concluded that during life a continuous transformation of lymphoid into red blood-cells takes place.

G. Bizzozero† found in the medulla of bone, besides colorless protoplasmic bodies, such with homogeneous, reddish-yellow nuclei, and also bodies about to divide, which contained two homogeneous reddish-yellow nuclei. He also interpreted these bodies as transitions of colorless to colored cells, and came to the conclusion that the medulla of bone was of importance in the production of colorless and red blood-corpuscles, and that the formations of the latter started from the nuclei of the former.

It is obvious that the formations described by these investigators are identical with those I had termed hæmatoblastic, which occur not only in the medulla of bone, but also in bone and cartilage in the normal process of ossification. The yellow lumps which all of us have seen are by no means blood-corpuscles, though under certain circumstances they may furnish the material for the formation of blood-corpuscles.

* Centralblatt für die med. Wissenschaften, 1868. Archiv der Heilkunde, x.
† Gazetta medica Lombarda, 1868 and 1869.

Based upon researches in cartilage and bone of birds, L. Schöney, in 1876,* makes the following statements:

"E. Neumann † has denied the new formation of red blood-corpuscles on the border of ossification of the cartilage. At the same time he draws attention to Aeby, who already in 1858 suggested such a new formation. From the quotation of Aeby's words, it follows that he only supposed the new formation on the border of ossification, as his researches in this direction did not yield positive results, whereas Heitzmann positively asserts the fact of such a new formation.

"E. Neumann's reasoning I cannot consider correct; he, f. i., could not understand that hæmatoblasts should stain with carmine, while perfect red blood-corpuscles remain unstained. Heitzmann claims that the hæmatoblasts are in a juvenile condition of the protoplasm, from which, after certain changes have taken place, red blood-corpuscles arise. Corpuscles may react on being stained, in a different way, in their youth and old age.

"E. Neumann, furthermore, makes a point of the absence of nuclei in hæmatoblasts, assuming, as he does, that blood-corpuscles in their juvenile condition must have nuclei, though they are destitute of such later. My own researches may also clear up this point.

"E. Metschnikow ‡ found in the impregnated and hatched germ of fowl, at first nucleated, slightly colored, and later, nucleated, distinctly colored, blood-corpuscles, and concluded that the latter had originated from the former. This conclusion is not fully justified, as it is possible that, from the same source, at first slightly and afterward deeply colored blood-corpuscles may arise and pass into the circulation without necessarily having directly changed from one into the other. The same reasoning also holds good for the blood-corpuscles of mammals. If at first nucleated and afterward non-nucleated blood-corpuscles are visible, who is willing to maintain that the latter have originated from the former, and that each red blood-corpuscle must have had a stage of nucleation?

* "Ueber den Ossificationsprocess bei Vögeln, und die Neubildung von rothen Blutkörperchen an der Ossificationsgrenze." Archiv für mikroskopische Anatomie. Bd. xii.

† Heitzmann's "Hæmatoblasten." Archiv für mikroskopische Anatomie, November, 1874.

‡ "Zur Entwicklungsgeschichte der rothen Blutkörperchen." Virchow's Archiv, 41 Bd., 1867.

"On watching specimens from the border of ossification of a growing chicken, we see within melted portions of the calcified basis-substance, homogeneous, shining lumps, in club-shaped spaces, inclosed by spindle-shaped elements. These spaces are not connected with perfect blood-vessels. The authors agree in considering such club-shaped formations as the first appearance of blood-vessels in the center of a medullary space. What are the shining corpuscles in the interior of a future vessel? What else than not fully developed blood-corpuscles?—therefore, hæmatoblasts. It is remarkable that these corpuscles have no nuclei, and corpuscles crowded in blood-vessels toward the bone-tissue, the connection of which with older blood-vessels is not yet evident, also want nuclei. Nucleated blood-corpuscles, so characteristic in birds, are visible only in deeper layers of the fully formed bone-tissue. If we admit that the youngest medullary formations are found in the ossifying borders of the cartilage, and that in the medullary spaces there are present corpuscles, to be considered as blood-corpuscles, we may readily accept the possibility that the nucleus is not an early, but rather a later, formation. This would agree with the statement of E. Brücke, concerning the formation of the nucleus in different other protoplasmic bodies. (See Fig. 30.)

FIG. 30.—OBLIQUE SECTION THROUGH THE BORDER OF OSSIFICATION OF THE CONDYLE OF FEMUR OF A YOUNG CHICKEN.

The central medullary space is surrounded by the calcified frame, *C*, of the hyaline cartilage, and in its middle there are several club-shaped spaces containing hæmatoblasts, *H*. In the lowest space, *B*, the red blood-corpuscles do not yet exhibit nuclei. Magnif. 700 diam.

"The specimen illustrated above admits of but one interpretation, viz.: that in fowls the first formed blood-corpuscles, the hæmatoblasts, have no nuclei; whereas complete red blood-

corpuscles have nuclei. The nucleus is evidently not a requirement of juvenile red blood-corpuscles.

"In full-grown birds such a new formation of blood-corpuscles does not occur. In a pigeon nine months old, the layer of globular cartilage-corpuscles is directly bounded by bone-tissue, containing medullary spaces filled with fat. The blood-vessels of these spaces at their upper ends, looking toward the cartilage, are looped. The intermediate stage of ossification of the basis-substance and new formation of blood-vessels and hæmatoblasts is absent. In still older animals, in which the layer of hyaline cartilage is much reduced in thickness, the upper ends of the medullary spaces toward the cartilage are closed by concentric systems of lamellæ of completely formed bone-tissue."

Hayem (see page 98) in 1877 described small shining lumps in the fluid of blood, more numerous in the fœtus than in the adult, which he, I think justly, termed "hæmatoblasts."

Red blood-corpuscles are very early formations of the middle layer (mesoblast) of the embryo. Probably they originate in every part of the body wherever there is living matter, especially in all varieties of that tissue which is exclusively supplied with blood-vessels, viz.: the connective tissue. Red blood-corpuscles are produced from lumps of living matter whenever, in the young, one variety of connective tissue is transformed into another—f. i., cartilage into bone. After the organism has reached full development, the production of colored blood-corpuscles continues in that variety of connective tissue which longer than any other remains in a juvenile condition, namely, the lymph-tissue. This tissue is present in large quantity in the body—the larger the younger the individual. It exists in all mucous layers, in the medulla of juvenile bone, in the lymph-ganglia, and in the spleen. Unfortunately, in consequence of former misapprehension of the nature and significance of this tissue, it bears the misnomer "adenoid tissue." That this tissue is a source of red blood-corpuscles during the entire life-time, will be demonstrated in the next article.

Experimental and Microscopical Studies on the Origin of the Blood-Globules. By A. W. Johnstone, M. D., Danville, Ky.*

The objects of this paper are to give the result of a repetition of Onimus's experiments on the "origin of the white blood-corpuscles," and to place on record an account of an undescribed method of development that is constantly

* "Archives of Medicine," vol. vi., August, 1881.

going on in the adenoid tissues. His conclusions are that the corpuscles have sprung up *de novo* from the blastema, and by analogy he argues that there is a spontaneous generation going on in serum wherever it is found. As given by Flint, these experiments on animals are as follows: The serum from quickly drawn blisters, after having been freed by filtration, etc., etc., from all its organized elements, is placed in bags of gold-beater's skin. These sacks are then placed in the subcutaneous tissues of rabbits, and after a sojourn of two or three days their serum is found to contain a variable number of leucocytes. I have repeated these investigations, and in two directions have pushed them farther than their author; that is, instead of the blastema, in the course of the experiments I used four different liquids, and in all cases, besides the fluids, I examined the gold-beater's skin after its removal.

In addition to the serum, I used a weak solution of chloride of sodium in water, a mixture of this with the white of an egg, and lastly the clear part of the egg alone. The animals used were cats; the length of experiments from seventeen to fifty hours; the thickness of the inclosing membranes was in most instances one, but in two cases two, layers of the gold-beater's skin. In all cases I examined both membrane and blastema before the introduction to the cat, and thus made sure that no organisms were present. My results were that in every case, except where I used a varnished membrane, I found leucocytes in the blastema, and wherever they were found in the liquid, the walls of the inclosing bag were sure to be crowded with the same organisms.

The only things that seemed to influence the number of the corpuscles were the condition of the containing membrane and the length of time the sack remained under the skin. If these conditions were the same, there were just as many corpuscles in the solution of chloride of sodium, or the egg mixtures, as there were in the serum. In the cases where the skin was doubled after a longer time than was ordinarily employed, a few corpuscles made their appearance in the blastema, a few were found in the inner layer of the bag, whilst the outer one contained a great many.

From these facts we are forced to the conclusion that the corpuscles migrated through the walls of the bags, just as they do to the interior of the catgut ligatures that are left in similar conditions.

This, however, is only a negative kind of proof, and for something positive I will ask the reader's attention to my recent study of the so-called *adenoid tissue*.

It is not necessary here for me to give the histology of the organs that contain this tissue, and to repeat that in the lymph-ganglia it is arranged into lymph follicles, lymph cords, and interfollicular strings; in the alimentary canal into follicles such as are contained by the tonsil, base of the tongue, pharynx, stomach, solitary glands, Peyer's patches, etc.; in the spleen into the ensheathing coats of the arteries, and the so-called Malpighian corpuscles, etc. But for our purpose, all that we need to know is that, wherever this tissue may be, there is a stream of fluid coming into it on one side, which, after working its way through the sponge-like mass, passes out on the other, and eventually empties into the blood.

The two questions to which we will now address ourselves are: Whence comes and what is the function of the "adenoid" tissue.

All histologists agree that in the animal kingdom we find but four varieties of connective tissue, and that they are the myxomatous, the fibrous, the cartilaginous, and the osseous. The myxomatous connective tissue is met

th almost exclusively in the earliest stages of development of the embryonal nnective tissue, and in transient fœtal organs, such as the umbilical cord d placenta. This tissue appears in two varieties: first, in the shape of a otoplasmic reticulum of greatly varying size, with nuclei at its points of tersection, the meshes of which hold the jelly-like mucoid basis-substance umbilical cord). In the centers of the meshes, globular and apparently olated bodies are seen. The other form consists of a delicate fibrous eticulum, having oblong nuclei at the points of intersection, the meshes being filled with single protoplasmic bodies (so-called "decidua cells" of the placenta), or with a mucoid basis-substance with scanty bodies (derma and mucosa of the embryo in the earliest stages).

Recent researches have proved that this mucoid basis-substance is not a structureless mass, but that it is pierced by a living reticulum, which is continuous with a smaller net-work pervading all protoplasmic formations. As the fibrous reticulum of myxomatous tissue is a protoplasmic formation, its fibers, too, contain a fine reticulum of living matter, which is also continuous with the fine reticulum of its neighbors. So the basis-substance, in either its mucoid or fibrous variety, differs from protoplasm only by a chemically altered substance within the meshes. This substance in the protoplasm is a liquid, in the basis-substance a semi-solid, though not strictly glue-yielding mass.

As has been known for a long time, comparatively low powers, when brought to bear on the adenoid tissue, demonstrate the presence of a delicate fibrous reticulum, which at the points of intersection is generally slightly thickened and flattened so as to present a plate-like appearance.

These intersections are sometimes provided with nuclei, and the meshes of the net-work are always filled with lymph-corpuscles. Although these corpuscles are so closely packed that they often flatten each other, still each one is generally separated from its neighbors by a narrow, light substance which is probably liquid.

Unless the lymph-corpuscles be torn apart by mechanical injuries, such as cutting, washing, etc., etc., they are all connected with each other by extremely delicate, grayish spokes, which traverse the intermediate substance in all directions. A like connection always exists between the lymph-corpuscles and the fibrous reticulum nearest to them.

Most authors claim that this fibrous reticulum of the adenoid tissue is structureless, and exhibits nuclei only at its points of intersection. This assertion must be based on Canada balsam specimens, for it makes all minute details fade away. My own specimens, cut from fresh lymph-ganglia, or such as had been preserved in a dilute solution of chromic acid, show a well-marked net-work in the fibrous reticulum, both in the unstained and in the carmine specimens.

While we are on this subject of the preparation of specimens, let me say, once for all, that if we hope to see the minute structure of this tissue, our sections must be cut from fresh or from chromic acid preparations, for alcohol or water destroys the details. If stained at all, it should be done with carmine, or, what is better, the one-half per cent. of chloride of gold. This last-named agent has a peculiar faculty for taking hold of the living matter of the most minute organisms and making it stand out in a very satisfactory manner. Lastly, I would state that glycerine seems to be the only mounting substance now known that will preserve tissues absolutely unchanged.

Reasoning by analogy, it seems that we are forced to conclude that adenoid tissue is myxomatous, and therefore a remnant of fœtal tissue. We know that the myxomatous tissue is abundant in the embryo, and relatively scarce in the fully developed fœtus. In the adult, the vitreous body was considered the only remnant of embryonal myxomatous tissue. To this, however, we should add the adenoid, and thus answer our first question.

To get a better idea of this tissue, let us turn to its most minute anatomy, and for the present we will confine our attention to its frame-work. As I

FIG. 31.—LYMPH-GANGLION OF CAT.

R, myxomatous reticulum, exhibiting in its interior a delicate reticulum of living matter; *G*, granules of living matter arising from the growth of the intersections of the contained reticulum; *V*, granules grown into vacuoled corpuscles and intermediate stages of development, *L*, full grown nucleated lymph-corpuscles, *M*, mesh of the myxomatous net-work, filled with lymph-corpuscles of all stages of development. Magnified 1200 diameters.

have already said, in the frame-work, which looks perfectly homogeneous under a 500, with a 1200 (immersion) we can readily recognize a delicate reticulum piercing nearly all its fibers and plates. In some places, even without the use of a staining re-agent, this net-work is just as plain as in the

corpuscles themselves, the only difference being that its meshes are a little wider than those in the globule. But the point to which I wish to draw particular attention is that the granules, at the points of intersection, vary very much in size. Sometimes, where they are seen along the edges of broad fibers, or in the centers of very fine ones, they give it a beaded appearance. At others they are so small that they are just barely appreciable. This inequality in size is most probably due to a growth that is constantly going on in these granules, and our finding different ones at different stages of it. (See Fig. 31.)

This process does not stop where the lump of living matter can be called a granule, but it keeps on until it has converted it into what is known as a corpuscle. This is accomplished by the smaller granule increasing until it has become so large that the fiber can no longer contain it without showing a slight bulging at the point where the granule lies. This is what gives the beaded appearance just referred to. But as the bead still grows, it protrudes more and more from the free surface of the fiber, until it has the appearance of a small homogeneous yellowish corpuscle sticking to the side of the fiber. The corpuscle is not separated from the fiber in this immature state, but retains a connection in the shape of very delicate grayish spoke-like threads, that can be traced directly to the granules within the fiber. This connection is constant in all the different-sized corpuscles, except the very largest, and in all probability is the route through which the corpuscle draws its nourishment. We can see no differences in these growing corpuscles until they are about three-quarters the size of a red blood-globule. Then, however, they seem to be divided into two classes. Whether there are two sets of fibers that produce the different corpuscles, or how else it is done, is more than I can say; but I am sure that, at the stage I have indicated, one set become more highly refracting than the other, and take more and more of the characteristics of a red blood-globule, which they eventually become. The others, however, follow the course that C. Heitzmann has described, as the elementary homogeneous granule takes in its development into a higher grade of protoplasm. After they reach the size I have already spoken of, a cavity containing a small amount of liquid forms, then similar excavations show themselves, until only a frame-work of the living matter is left between the vacuoles. There are communications established between these cavities, and the frame-work is transformed into a net-work with thickened points of intersection, which are the granules.

With this view of the development of protoplasm we are better able to understand the meaning of the vacuoled corpuscles that we so often meet with. But the different sizes of the corpuscles, the different numbers of their granules, and the varying conditions of their nuclei and reticula, speak for themselves. They are the different stages through which an original granule of the fine reticulum contained by the fibrous net-work is developed into a full-grown lymph-corpuscle.

This is further substantiated by the fact that the connection, already described, between the granule that has just passed to the outside of the fiber and the reticulum within it, is kept up through all sizes and shapes of corpuscles, until the full-grown condition is reached. Then, however, this attachment is severed, and the globule passes away with the lymph stream in which it has been bathed so long. This is true of both sets of corpuscles, and can be shown as well in the young red as in the white. Thus we add a new proof

to the old idea that a red globule is nothing but a mass of protoplasm containing hæmoglobine within its meshes; for the elaboration of this subject I refer to the researches of L. Elsberg.

The organs that I have used in these investigations are the lymphatic ganglia of man, horse, and cat, the spleen of man and cat, as well as the tonsil and thymus gland of children. The characteristics of the adenoid tissue were found to be the same in all, the principal differences being in the proportion of red to white globules. In the tonsil and lymphatic ganglia, the red are very scanty, though they can be found in most fields; but in the spleen they are far more frequent. In this organ, like the rest, the corpuscles are formed by the development of the granules of the net-work within the frame, and not by budding of the endothelial plates, as claimed by some. We are now ready to give the reason for the lymph of the efferent vessels containing so many more corpuscles than that of the afferent, as well as to say where the few red globules that are found in the lymph of the thoracic duct come from. The lymph stream, as it passes through each successive ganglion, carries along an increased number of the fully grown elements that have become detached from the parent fiber, and eventually empties them into this duct, through which they reach the blood.

In answering these questions, we are also giving the function of the adenoid tissue, which is to produce the corpuscular elements of the blood.

It has been known for a long time that as age advances the adenoid tissue becomes more and more scarce, and that the mucous layers and other organs that were once so rich in it, at extreme old age present scarcely a trace. In reality, the thymus gland may be taken as the type of the whole class. For while their degeneration is by no means so rapid, still they all show a tendency to follow its example. This is most strikingly shown in the history of Peyer's patches, as has been brought out by the study of typhoid fever. From this we would conclude that a young animal is the best subject for the study of the adenoid tissue. This I can testify is the case, for as age advances the granules of the reticulum within the fibers become more scanty, and the reticulum itself is by no means so rich as in the early days of life. Should it ever be conclusively proved that the white blood-corpuscles share in the formation or repair of the structures of the body, we would then have the complete chain of their history; for we are now sure that they represent only one stage of a development that is going on as long as life lasts, and I am not inclined to believe that this stage is the highest of the series.

The conclusions that I have drawn from these studies are:

1st. We must have more and better proof before we can believe that a lymph-corpuscle ever arises from a blastema.

2d. That both red and white blood-corpuscles are developed from the granules of the reticulum of living matter within the fibers of all adenoid tissues.

3d. That in different organs there is a difference in the proportion of red to white globules that are produced.

4th. That the adenoid tissue is myxomatous, and, properly speaking, a remnant of fœtal life.

5th. That this tissue is stored-up material, from which the blood-corpuscles are made throughout life.

6th. That it is highly probable that the exhaustion of this material plays an important part in senile atrophy, and the other torpid conditions of the aged.

VI.

TISSUES IN GENERAL.

ORIGIN, DEFINITION, AND DIVISION OF TISSUES.

ORIGIN. All complex organisms, the higher developed animals, originate from an ovum of the female impregnated by the admixture of spermatozoids of the male. The ovum, inclosed by a hyaline layer (zona pellucida of Von Baer), is composed of living matter in reticular arrangement (the germ of Remak), which contains a nucleus-like body, the vesicula germinativa, with a varying number of coarser granules, the nucleoli, the maculæ germinativæ. In mammals and some amphibia, the germ, *in toto*, is transformed into the animal, whereas in the eggs of birds, scaly amphibia, and osseous fishes, a portion of the germ is changed to yolk, which serves as a pabulum.

After the spermatozoids have entered the germ—viz.: after fructification has taken place—its living matter increases rapidly, the vesicula germinativa disappears, and the germ, by a process of division, splits at first into two portions, separated from each other by a light narrow rim, but connected by extremely delicate filaments, which traverse the light rim. Each half of the germ splits into a number of lumps, which, in the same manner as the first half, remain connected; thus the segmentation of the ovum results in the formation of numerous corpuscles, which by collecting in a flat layer represent the germinal disk of Pander, in

the germ of the impregnated egg of the chicken. The segmentation was first observed by Prevost and Dumas (1824) in the ovum of frog; by Coste (1848) in the ovum of fowls; and by Bischoff (1842) in the ovum of mammals. According to this last-named observer, the subdivision into smaller elements in the rabbit's germ does not go on uniformly throughout its whole extent, inasmuch as in the germ a cavity is formed, around which the elements of segmentation accumulate, in order to build up the germ-membrane proper, with a slightly thickened spot, the germ-hill of Von Baer.

The first differentiation of the germ-disk, or the germ-membrane, consists in the formation of layers, of which at first two, shortly afterward three, are recognizable. The formation of such layers became known first through the researches of Caspar Friedrich Wolff (1768), who claimed that the whole system of the intestines is developed from simple laminæ. Pander, in 1817, perfected the theories of Wolff; he knew that after hatching had continued for twenty-four hours, three easily separable layers could be found in the germ-membrane. Von Baer, in 1822, described four layers, of which the two upper he termed the animal, the two lower ones the vegetative. Remak, in 1855, maintained that the germ-membrane of the impregnated but unhatched egg consists of two layers, and upon hatching the lower is again split into two layers, the lower of which lines the one above it like an epithelial cover. Having ascertained the individuality of each of these three layers, he endeavored to find out their relation to the developing organs; he called the upper layer the horny or sensorial; the middle layer the motorial and germinative; the under layer intestinal and glandular. According to S. Stricker's researches (1860–1870), the original under layer of Remak consists—at least above the germ-cavity, and before the middle layer has made its appearance—of only a single stratum of flattened cells, and the formation of the middle layer is due to the immigration between the two layers of new cells. He termed the upper layer of Remak the combined horny and nervous layer, as he found that in batrachia the horny layer is quite distinct from the nervous layer, the former being uniformly thin; the latter, on the contrary, thickened even in the earliest stages in that part where later the brain is formed. He is unable to confirm, despite of Remak's positive assertions, that nervous elements are also developed from the middle layer.

Stricker ("Manual of Histology," American edition, 1872), in speaking of the development of the fowl's germ, says: "The cells of the under layer change their form and arrangement during the first hours of incubation. They become flattened, and, when seen in transverse section, appear spindle-shaped. Hence, after incubation has gone on for a few hours, we can ascertain, beyond even the shadow of a doubt, that there are two and only two layers. . . . The under layer, immediately after its separation from the subdivided germ, consisted in some places of a single thickness of cells, while in other places, in a transverse section, small heaps of cells could be recognized projecting from the layer. . . . Peremeschko, however, has made the communication that the large granular cells lying on the bottom of the germ-cavity increase very considerably in numbers during the first hours of incubation. Now, since with this increase in numbers there is not at the same time a corresponding diminution in size, it is very natural to suppose that the cells which project from the under germ-layer fall to the bottom of the cavity. This supposition appears all the more probable when we recall the fact that some of the elements of segmentation which are situated in the lower portion of the germ, remain lying at the bottom of the cavity at the time when the germ, in the production of this very cavity, separates itself from the subjacent parts. . . . We are led to conjecture that the process is one of translocation; that the granular bodies, which before lay at the bottom of the cavity, have found their way to the space between the two first germ-layers." Stricker, based upon Oellacher's researches, says that similar relations are also found in the trout's germ.

At present, investigators agree that the body of vertebrates is at first a flat sheet, consisting of three main layers, for the designation of which the following names have been proposed: Exoderma, Mesoderma, and Entoderma, or, preferably, *epiblast*, the upper layer; *mesoblast*, the middle layer; and *hypoblast*, the under layer. Of these, the epiblast and hypoblast are very thin, composed of but one layer of plastids, whereas the mesoblast is a bulky heap of plastids, all of which are interconnected and represent the main mass of the future organism. As the originally flat sheet of the germ becomes curved downward, so that the two lateral halves are bent toward the median line, where they grow together, cavities are formed in the interior of the germ, which are lined by the under layer and its derivatives. The horny layer furnishes the external covering of the body and the lining of the external glands, while the under layer provides the lining of the intestinal cavity and its glandular organs. Linings of this description are called "epithelia," and it follows that the epiblast and hypoblast give rise to all epithelia, viz.: the epiblast to those of the skin and its epithelial formations (including the crystalline lens); the hypoblast to those of the intestines and their glandular elongations and accumulations. The main bulk of the body

is a product of the mesoblast; from it proceed the tissues termed connective tissue, which alone contains blood and lymph-vessels, muscles, and nerves, the latter arising from the uppermost portions of the mesoblast.

DEFINITION. In comparing the earliest formations of the germ with a single plastid formerly called a "uni-cellular organism" or a "protoplasmic body," such as the amœba, valuable hints may be obtained as to the significance of the three germinal layers. The amœba is covered by an extremely thin layer of living matter. If the amœba be flattened out and bent, its cover will represent the upper and under thin layer of the germ, which exclusively serves as an investing layer of both the outer surface and all cavities of the body, being directly or indirectly connected with the outer world. The main bulk of the amœba is living matter in reticular arrangement, with thickened points of intersection of the threads of the net-work; this matter, retaining in the mesoblast and its derivations its reticular shape, furnishes in higher organisms the tissues, as a result of a sort of division of labor. The nature of the tissues is determined, first, by the manner in which the living matter is distributed, and, secondly, by the chemical changes of the fluid contained in the meshes of the reticulum.

Tissues are complex formations of living matter in a net-work arrangement. The meshes of the net-work contain a liquid which allows the living matter to exhibit contractility in a high degree, as in muscles and nerves, or the net-work contains a more or less solidified basis-substance, which limits its contractility, as in the connective tissue. The latter, on account of the presence of this basis-substance, mainly serves as a support for the more active tissues (muscles and nerves), and as a carrier of liquids in closed spaces.

DIVISION. According to this view there are but four elementary tissues in the animal body. All these are interconnected and built upon one and the same plan.

1. *Connective tissue.* In this the reticulum of living matter contains in its meshes a more or less solid, nitrogenous (glue-yielding) basis-substance; while points of intersection rich in living matter, suspended in a liquid, represent the connective tissue corpuscles. Of all tissues only the connective tissue carries in closed vessels the liquids which serve for nutrition, such as blood and lymph. Aside from this, and acting as support for other tissues, its physiological activity is relatively small.

2. *Muscle tissue.* The reticulum of living matter at its points of ıtersection consists of more or less regularly distributed large rismatic, cylindrical, or granular thickenings (sarcous elements), onnected by thin filaments, while the meshes contain a liquid which admits of powerful contractions of the living matter in large territories. This tissue is the motor apparatus proper. It is accompanied by and attached to connective tissue, carrying the vessels.

3. *Nerve tissue.* Here the living matter is arranged in the shape of either a very delicate reticulum, with very small points of intersection (ganglionic corpuscles, gray matter), or delicate solid cords (axis-cylinders), while the meshes contain a liquid which allows the living matter in limited territories to contract rapidly. This tissue serves as an apparatus of sense-impression, intellect, and sensory and motor conduction. It is largely accompanied by and mixed with connective tissue, carrying blood-vessels.

4. *Epithelial tissue.* The reticulum of living matter is very delicate, and arranged in flat layers, which at certain regular intervals contain a horny cement substance. The function of epithelial tissue is to cover the surface and the cavities of the body; it alone serves as apparatus of secretion, and for the formation of the essential parts of reproduction—spermatozoids and ovum.

THE RELATION OF LIVING MATTER TO THE INTERSTITIAL SUBSTANCE.

This article is translated from a publication in German made in 1873,* with some unimportant statements omitted.

In my studies of bone and cartilage,† I have demonstrated that the cartilage-corpuscles send numerous offshoots into the basis-substance termed "hyaline," and that these offshoots freely anastomose and connect the "cells" with one another. The material was furnished by fresh living hyaline cartilage, silver-tinction, gold-tinction, normal calcification of cartilage, and inflammatory calcification after simultaneously wounding cartilage and bone.

The deposition of lime-salts in hyaline cartilage, in conse-

* "Untersuchungen über das Protoplasma. II. Das Verhältniss zwischen otoplasma und Grundsubstanz im Thierkörper." Sitzungsber. der Akademie Wissensch. in Wien. Mai, 1873.

† "Studien am Knochen und Knorpel." Med. Jahrbücher, 1872.

quence of inflammation, especially served for bringing to view a delicate reticulum in the basis-substance, as such a deposition took place in the chondrogenous substance, while the protoplasmic bodies and their offshoots remained unchanged. This reticulum corresponded with the light (negative) figures obtained by treatment with nitrate of silver and with the violet (positive) figures after gold-tinction.

I wish to add a few more observations concerning the life and the structure of cartilage-corpuscles.

If we examine a thin section from the condyle of femur of a middle-sized rabbit, in a one-half per cent. solution of chloride of sodium, or a little serum of blood, with high amplifications, we will see in many cartilage-corpuscles a structure identical with that I have described in colorless blood-corpuscles of man. The nucleus, if visible, appears either homogeneous or constructed of a dense reticulum of a shining substance,—the living matter,—and inclosed by a continuous layer of the same substance. The nucleus sends delicate conical filaments into the reticulum of the corpuscle, and the points of intersection of this reticulum are thickenings, granules, or lumps of living matter. In the narrow light rim between the protoplasm and the basis-substance we also see delicate spokes emanating from the cartilage-corpuscles, which are lost to sight in the finely granular but in some places distinctly reticular basis-substance.

If we heat a fresh specimen to 30–35 degrees C. (86–91 degrees F.), we can observe in cartilage-corpuscles having a reticular structure a continuous though very slow change in the configuration of the living matter. Points of intersection flow together into homogeneous lumps; the latter again are differentiated into a reticulum, and such change continues until rest of the living matter occurs—these changes in the reticulum not noticeably altering, however, the general shape of the corpuscle.

A direct proof is thus obtained that cartilage-corpuscles are alive, which was made probable by R. Heidenhain and A. Rollett by observations of cartilage-corpuscles of the frog and newt on the application of induced electricity.

A one-half per cent. solution of chloride of gold is a suitable re-agent for plainly bringing to view the structure of cartilage-corpuscles,* and for this purpose a slight tinction is sufficient. (See Fig. 32.)

* Method of J. Cohnheim. "Ueber die Endigung der sensiblen Nerven in der Hornhaut." Virchow's Archiv, 38. Bd. 1867.

To these observations in cartilage I add a series of researches in different other tissues of the body.

Medullary tissue. The medulla between the trabeculæ of a shaft-bone of a newly born pup consists of lumps of protoplasm, which are imbedded in a homogeneous basis-substance. These lumps vary greatly in their aspect. However the corpuscle may look, invariably spokes emanate from it which pierce the surrounding light zone radiatingly, and are visible with high amplification only. Where the lumps are near each other, the spokes directly connect them; if, on the contrary, the lumps are separated from each other by broad layers of basis-substance, the spokes of a lump enter the latter, and in most instances disappear. (See Fig. 33.)

The elements of the medulla termed "osteoblasts" by Gegenbaur* exhibit the same features both in the medullary spaces of

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FIG. 32.—CARTILAGE CORPUSCLES FROM THE CONDYLE OF FEMUR OF A NEW-BORN PUP. [PUBLISHED IN 1873.]

Chromic acid specimen slightly stained with chloride of gold. C^1, corpuscle with one compact, vacuoled nucleus, C^2, with a pale heap of granules above it; C^3, with two nuclei and several heaps of granules. Magnified 1000 diameters.

newly born pups, close to the bony trabeculæ, and in the vascular canals of shaft-bones of older animals.

Where the elements lie close to the bone-wall, they are separated from the latter by a light rim, and the filaments, springing

* Jenaische Zeitschr. f. Mediz. und Naturwissensch. I. Band. 1864. This observer knew already delicate offshoots, like cilia, emanating from osteoblasts.

from the medullary corpuscles, pass through the rim into the basis-substance. Where the medullary corpuscles are near the border of a vessel, their offshoots traverse the light, perivascular rim and inosculate with the wall of the blood-vessel.*

Upon slight gold tinction of chromic acid specimens previously exposed to water, the spokes exhibit a distinct violet color. The longer the solution of gold acts, the more distinct will be a differentiation in the basis-substance. The protoplasmic lumps at last appear as dark violet, densely reticular corpuscles with numerous

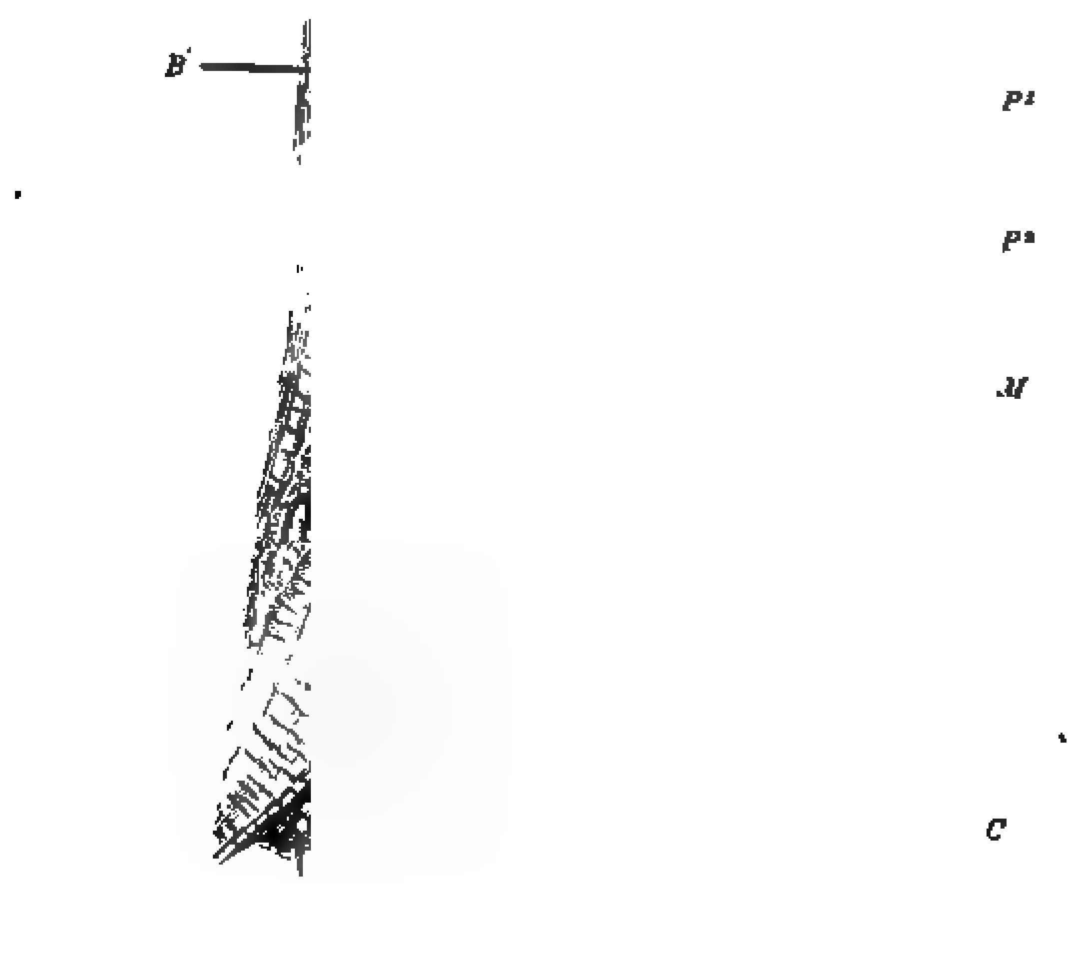


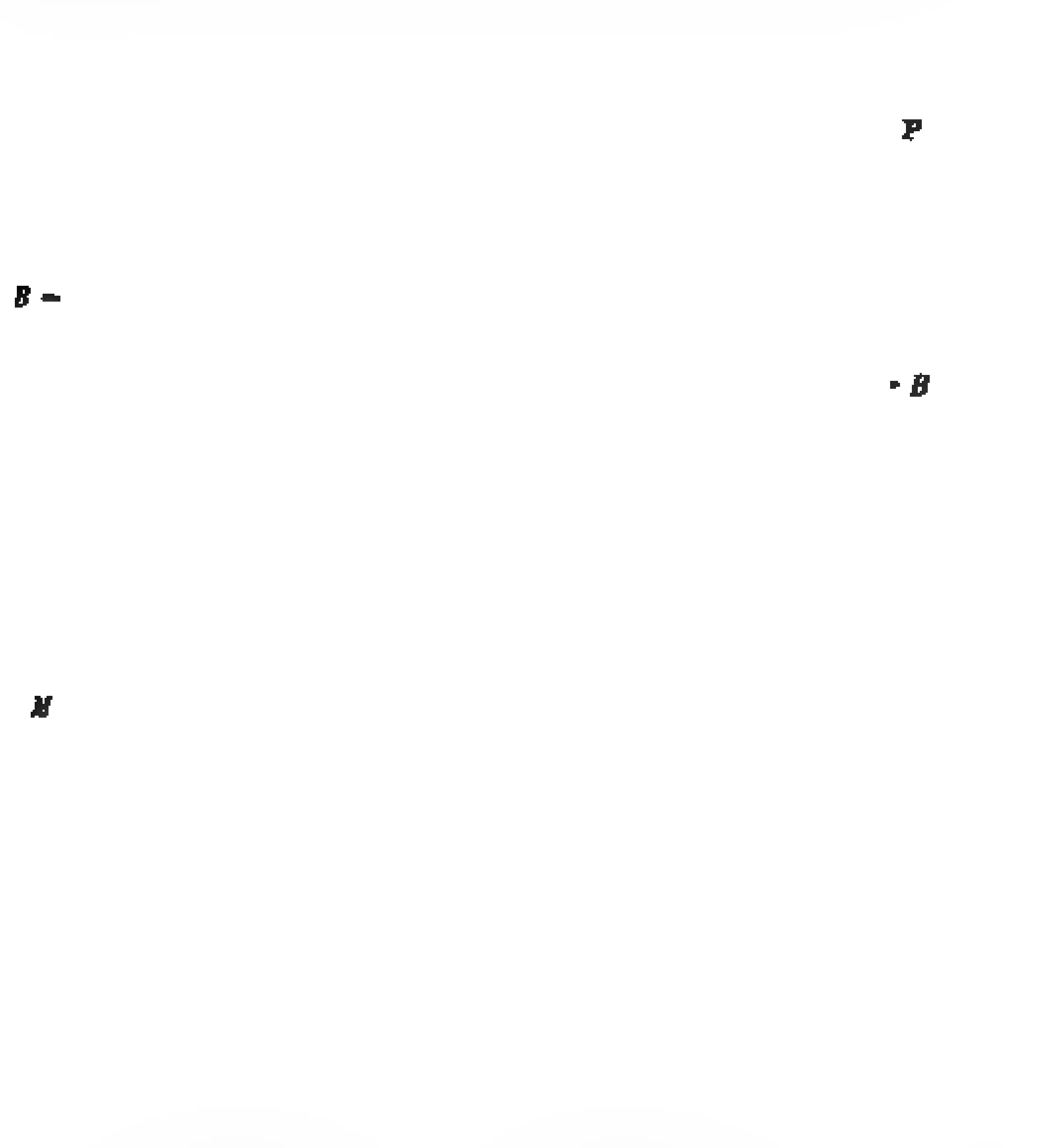
FIG. 33.—MEDULLARY TISSUE FROM A LONGITUDINAL SECTION OF THE FEMUR OF A NEW-BORN PUP. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

B, bone-corpuscle; P^1, vacuoled plastid; P^2, reticular nucleated plastid; *M*, apparently structureless basis-substance; *C*, capillary blood-vessel. Magnified 800 diameters.

delicate radiating spokes, which blend with a partly coarse, partly delicate, reticulum. (See Fig. 34.)

* Confr. "Ueber die Rück- und Neubildung von Blutgefässen im Knochen und Knorpel." Med. Jahrbücher, 1873.

Γhe basis-substance is traversed by a reticulum which has for ıts of intersection of its threads coarser and finer granules. tracing the action of the gold solution, we can satisfy ourselves t the densest reticulum with the smallest mesh-spaces belongs the yellowish, shining medullary elements, and the larger let lumps are either homogeneous nuclei or nucleoli. The st delicate reticulum with smallest granules as points of intertion, and the largest mesh-spaces, corresponds to those places



ı. 34.—MEDULLARY TISSUE FROM A LONGITUDINAL SECTION OF THE FEMUR OF A NEW-BORN PUP. THE BONE-TISSUE DECALCIFIED BY CHROMIC ACID, AND THE SPECIMEN INTENSELY STAINED WITH A SOLUTION OF CHLORIDE OF GOLD. [PUBLISHED IN 1873.]

bone-corpuscles, *P*, partly vacuoled, partly reticular plastids, *M*, the basis-substance xhibiting a reticular structure. Magnified 800 diameters.

he medullary tissue which, in the unstained condition of the cimen, appeared as an apparently homogeneous and structurebasis-substance.

Tissue of the Umbilical Cord. Longitudinal sections of the human umbilical cord, hardened in a chromic acid solution, exhibit, as is well known, a striated or fibrous structure. The fibers are densest at the periphery of the cord and around the blood-vessels, and these layers are interconnected by a relatively coarse reticulum of fibers, the meshes of which contain a homogeneous substance. In the fibrous layers we meet with large, nucleated, freely branching protoplasmic masses, also with smaller, spindle-shaped bodies, and with very small protoplasmic cords and lumps, devoid of nuclei. In the mesh-spaces, traversed by a few fibers which the cutting has partly torn, we encounter apparently isolated globular corpuscles, having one or several nuclei, but no offshoots.* The amount of living matter in the protoplasmic bodies is variable. We find compact lumps characterized by a nearly homogeneous structure, considerable luster, and yellow color; furthermore, coarsely and finely granular corpuscles, with either homogeneous, shining, or finely granular pale nuclei, some containing nucleoli; lastly, very pale, delicately granular bodies destitute of both nuclei and a marked boundary line toward the basis-substance. The periphery of all these corpuscles, while they are in connection with the tissue, looks more or less scalloped or thorny, and the same is the case with their nuclei.

Upon rubbing a fresh umbilical cord with a stick of nitrate of silver, and exposing the specimen, kept in water, to the daylight, it will soon become brown.†

Longitudinal sections of an umbilical cord colored in this way exhibit, even with lower amplifications, numerous many-shaped light and colorless fields in the brown basis-substance. High amplifications demonstrate that the light fields in different directions send branches into the basis-substance,‡ and that from

* For reference: Rud. Virchow's "Cellularpathologie," 4 Aufl., 1871. Weisman, "Zeitschrift für rat. Mediz." 3 Reihe, Bd. xi., 1861. K. Köster, "Ueber die feinere Structur der menschl. Nabelschnur," Würzburg, 1868. Köster found the globular corpuscles in the mesh-spaces, and the spindle-shaped cells near the spaces without fibrils, to be amœboid.

† Method of F. von Recklinghausen ("Die Lymphgefässe und ihre Beziehung zum Bindegewebe." Berlin, 1862). Specimens containing black, granular precipitations I consider as useless. The features described can be observed only when the basis-substance is stained light or dark brown, and the fields corresponding to the protoplasmic bodies are colorless.

‡ Köster *(l. c.)*, by means of the silver tinction, brought to view the larger light fields only.

hese light fields and their offshoots a delicate varicose ılum starts, which traverses the whole of the brown basis-ance. (See Fig. 35.)

light gold tinction shows that the violet nucleated bodies their coarser offshoots correspond, both in size and shape, the large light fields brought to view by nitrate of silver. pecimens deeply stained with chloride of gold, we observe , from each dark violet corpuscle and its offshoots, numerous

35.—Longitudinal Section from the Cortical Portion of the Human Umbilical Cord, Stained with Nitrate of Silver. [Pub-ished in 1873.]

B, larger and smaller light spaces traversing the brown basis-substance, which every-ere is pierced by a delicate light reticulum. Magnified 800 diameters.

delicate dark violet filaments proceed, penetrating a vari-granular net-work. The latter traverses the basis-substance

in a direction mainly vertical to that of the fibers. Even a single fiber can be seen to be composed of alternating light violet and dark violet portions. (See Fig. 36.)

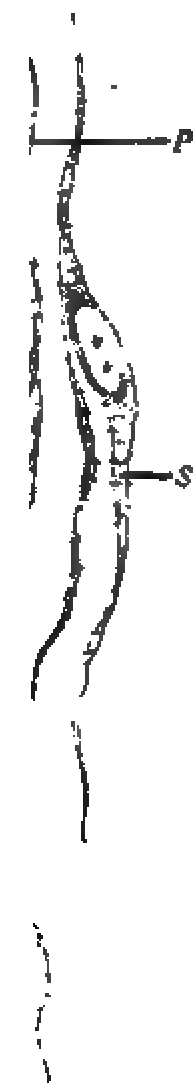


FIG. 36.—LONGITUDINAL SECTION FROM THE CORTICAL PORTION OF THE HUMAN UMBILICAL CORD, INTENSELY STAINED WITH CHLORIDE OF GOLD. [PUBLISHED IN 1873.]

P, the plastids (protoplasmic bodies) with nuclei. *S*, smaller spindle-shaped plastids, composing the basis-substance; *F*, torn fibrilla, with an alternating light and dark stain. Magnified 800 diameters.

Numerous torn fibers originate from bipolar nucleated lumps, and each fiber appears to be pierced by a dark violet reticulum.

Tissue of Tendon. Similar features are found in the tendon. On rubbing the silver stick over the tendon Achillis of a freshly killed dog several years old, or of a grown rabbit, exposed to daylight, the brown tinction will appear after a while.

With lower powers we recognize in longitudinal sections of a tendon-bundle numerous narrow, spindle-shaped light fields,

dark-brown border of which is vertically perforated by light ›s, while the surrounding basis-substance looks uniformly ›wn and homogeneous.* Toward the periphery, the light ds are larger and often longitudinally forked; in the peri-ıdinous tissue they are very numerous, many-shaped, and ›arated by narrow, brown fields, or streaks of the basis-bstance.

High amplification shows that from the periphery of the light lds and their offshoots delicate light lines arise in a vertical rection, which blend with a varicose reticulum throughout the sis-substance, and thus connect each larger uncolored field th its neighbors. (See Fig. 37.)

ᵌ. 37.—LONGITUDINAL SECTION OF THE TENDO ACHILLIS OF A GROWN DOG, STAINED WITH NITRATE OF SILVER. [PUBLISHED IN 1873.]

S^1, light branching field, with a pale, dim nucleus, S^2, offshoot of a light field in the dle of basis-substance; S^3, bifurcation inclosing a narrow peg of basis-substance; *B*, dark wn basis-substance pierced by a mostly rectangular light reticulum. Magnified 800 meters.

Slight gold tinction reveals the identity of the pale violet odies with the protoplasmic corpuscles seen in chromic acid pecimens; they are identical, as regards their shape, also, with e negative fields obtained by silver tinction.† After intense old-stain, the striated basis-substance looks pale violet. There

* V. Recklinghausen *(l. c.)* also has observed anastomosing light fields in › silver-stained tendon.

† In this respect I concur with Giulio Bizzozero (Rendiconti del R. Isti-o lomb. delle scienze, 1869) and Paul Güterbock (Centralblatt für die d. Wissensch., 1870).

are dark violet, in part branching bodies in it, which send dark violet filaments into the basis-substance, mainly at right angles. Where the tendinous tissue is torn into bundles or single fibers, we easily recognize the dark violet reticulum, and in each single fiber the pale violet basis-substance contains, at irregular intervals, dark violet granules. On the border of some fibrous bundles small scallops protrude. The cross-section of a small bundle shows two kinds of formations: one granular, partly branching, dark violet; the other, homogeneous, colorless, or pale violet. (See Fig. 38.)

Tissue of the Periosteum. In chromic acid specimens of the periosteum of shaft-bones of grown dogs and cats, the light

FIG. 38.—LONGITUDINAL SECTION OF THE TENDO ACHILLIS OF A GROWN DOG, DEEPLY STAINED WITH CHLORIDE OF GOLD. [PUBLISHED IN 1873.]

P, the branching tendon-corpuscles, with light nuclei; *B*, bundle with distinct rectangular dark violet filaments; *F*, single dotted fibrillæ, *TS*, transverse section of a bundle. Magnified 800 diameters.

basis-substance, partly striated, is composed either of rhomboidal plates or of broad ribbons, which may exhibit a mosaic of rhombs. These formations are intermixed and interlaced in a vertical or oblique direction.

The variety of basis-substance consisting of broad ribbons is met with, as a rule, on the surface of the bone,* while the other

* The protoplasmic layer between periosteum and bone, which Th. Billroth (Archiv für Klinische Chirurgie, Bd. vi.) has termed "cambium," exists in juvenile animals only.

varieties prevail at the periphery of the periosteum, blending with neighboring tissues. The ribbons are separated from each other in a longitudinal direction by straight so-called elastic fibers, which render each ribbon rhomb-shaped. At the corners of the rhomb, the elastic fibers anastomose with each other in acute angles. A broad ribbon is not infrequently subdivided by elastic fibers into smaller rhombs.

FIG. 39.—LONGITUDINAL SECTION OF THE PERIOSTEUM OF THE FEMUR OF A GROWN DOG, STAINED WITH NITRATE OF SILVER. [PUBLISHED IN 1873.]

C, light spaces corresponding to the plastids, all of which are interconnected. *MT*, smooth muscle fibers of an artery in transverse section; *ML*, the same in longitudinal section; *E*, endothelium. Magnified 800 diameters.

The protoplasmic bodies are spindle-shaped in the striated, rhomboidal in the rhomb-shaped, and oblong in the ribboned basis-substance. In the interstices between the layers similar

corpuscles are imbedded. Properties common to all of these corpuscles are: they lie in cavities of the basis-substance, their periphery is scalloped, and they are possessed mostly of one nucleus. The nucleus and nucleoli look exactly like those of colorless blood-corpuscles.

In the basis-substance, stained brown by nitrate of silver, light fields of varying shape appear, which behave like those of the umbilical cord and the tendon. Here, too, the basis-substance is traversed by branching lines, which interconnect the large light fields. (See Fig. 39.)

Slight gold tinction of the periosteum brings to view delicate radiating scallops at the periphery of the corpuscles, and delicate vertical filaments in the interstices between the rhombs. The shining elastic ledges are transversely striated, being pierced by violet filaments. Deep gold-stain shows a dark violet reticulum throughout the basis-substance, just as in other varieties of connective tissue.

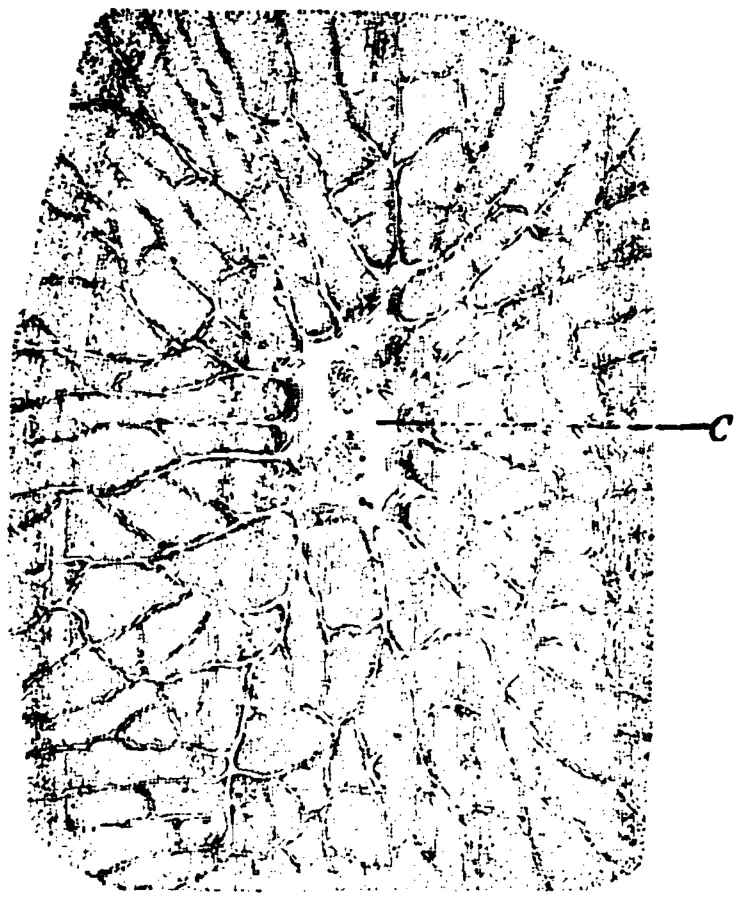


FIG. 40.—BONE-CORPUSCLE FROM A PURPOSELY WOUNDED SCAPULA OF CAT—THIRD DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1872.]

c, the nearly homogeneous plastid, with numerous ramifying offshoots. Magnified 800 diameters.

The *perichondrium* in all essentials is identical in its structure with the periosteum. Where *fibrous cartilage* blends with perichondrium, as on the lateral surfaces of the condyles of femurs of younger animals, the gold tinction evidences a dense reticulum of offshoots of the corpuscles of fibrous cartilage.

Tissue of bone. The basis-substance of juvenile bone is striated, that of older bone lamellated. The lamellæ are plates separated from each other by a non-calcified basis-substance, and each lamella is composed of flat, oblong lenticular masses, which are curved according to the lamella and contain one central bone-corpuscle.

In the earliest stages of inflammation of bone, the protoplasma swells so that, without any re-agent, numerous offshoots of the bone-corpuscles become visible, which freely anastomose and pro-

duce a delicate reticulum throughout the basis-substance. (See Fig. 40.)

Blood-vessels. Fig. 39 represents an artery from the silver-stained periosteum of a grown dog, in which we recognize that the brown basis-substance of the adventitial connective tissue, the cement-substance between the spindle-shaped muscle fibers, and the cement-substance between the endothelia, are all traversed by light lines, which interconnect the light fields corresponding to these formations.

Gold-stains bring to view, in the interstices between the single elements, conical filaments which connect all. The walls of capillaries of the compact substance of shaft-bones are, by means of filaments, in direct connection with the neighboring corpuscles, both of medulla and bone. These filaments penetrate the space around the hollow protoplasm of the vessel, the "perivascular lymph-space" of authors.

Muscle-tissue. In continuous layers of *smooth muscle*, both in the fresh condition and after the gold stain, we see that from each spindle arise numerous spokes, which, after having pierced the surrounding cement-substance, inosculate with the neighboring spindles. In such spindles, especially from the muscular wall of the blood-vessels of the umbilical cord, there is an accumulation of living matter which renders the corpuscle nearly homogeneous and highly refractive. In very shining spindles there are no nuclei. Wherever nuclei are seen, they are by means of conical spokes connected with the reticulum of living matter of the corpuscle.

The examination of *living striated muscle* from the thigh of the water-beetle (Hydrophilus) or craw-fish (Astacus) shows that the distribution of the contractile or "main" substance varies greatly. In opposition to the conceptions of W. Krause,* V. Hensen,† Th. W. Engelmann,‡ and others, I adopt the view of E. Brücke,§ viz., "that the sarcous elements do not exist as solid and unchangeable masses in the living muscle, but are groups of molecules arranged in columns of a varying configuration at the

* "Ueber den Bau der quergestreiften Muskelfaser." Zeitschrift f. rat. Medizin, 1868.

† "Ueber ein neues Structurverhältniss der quergestreiften Muskelfaser." Arbeiten des Kieler physiolog. Institutes, 1868.

‡ "Mikroskopische Untersuchungen über die quergestreifte Muskelsubstanz." Pflüger's Archiv, 1873.

§ "Untersuchungen über den Bau der Muskelfasern mit Hülfe des polar. Lichtes." Denkschriften d. Wiener Akademie d. Wissensch., Bd. xv.

moment of death." I am unable to see in the living, striated muscle anything else than in the living protoplasma in general—namely, granules and heaps of granules of living matter, the sarcous elements, and between these a non-contractile interstitial substance.

Whatever form the distribution of the contractile substance may give rise to, we can prove that every granule and every sarcous element is in all directions connected with its neighbors by means of delicate gray filaments piercing the interstitial substance in vertical and transverse directions. From each so-called "muscle-nucleus," and in case the nucleus is surrounded by protoplasm, from the latter, emanate delicate conical threads, which, after having penetrated the narrow light rim, blend with the neighboring sarcous elements. (See Fig. 41.)

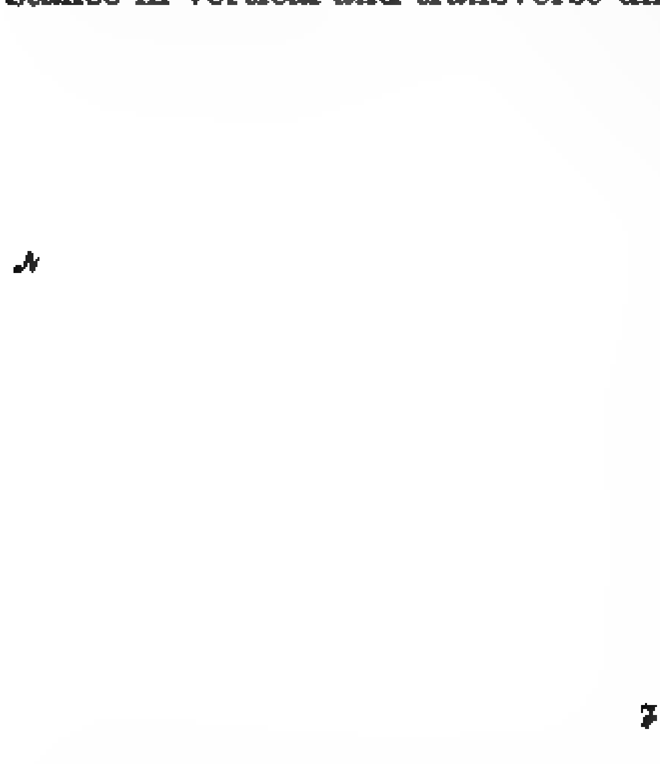


FIG. 41.—PORTION OF THE FRESH THIGH-MUSCLE OF HYDROPHILUS PICEUS. [PUBLISHED IN 1873.]

N, nucleus, *G*, granules in the longitudinal direction of the nucleus. Magnified 800 diameters.

In gold-stained specimens these features are far more striking than in fresh muscle, as the chloride of gold, acting for a sufficient length of time—viz., twenty to forty minutes,—stains the contractile substance of muscle violet.

Structure-elements of the Nervous System. Thin sections from the cortex or the main ganglia of a grown, recently killed rabbit are the best specimens for examination with high powers of the microscope. The section may be transferred to the slide without or with the addition of a preserving fluid: in the latter case, a very dilute solution of bichromate of potash is preferable, because, as proved by A. Rollett, this does not alter the structure of protoplasm. Layers of protoplasm, with numerous formations like nuclei, ganglion-corpuscles of varying shape, and non-medullated* nerve-fibers of different size are seen. The living matter in the formations termed nucleoli, being compactly accumulated, is homogeneous, and has a yellowish luster; while

* The original reads by mistake "medullated."

in the protoplasma of all structure-elements of the nervous system it is distributed in thin layers as granules and lumps, and is of an opaque gray color. All granules and lumps of the living matter are interconnected by delicate radiating spokes. (See Figs. 42 and 43.)

In the ganglion-corpuscles, especially in their nuclei, the spokes have been observed by a large number of investigators,* who interpreted these spokes as belonging exclusively to ganglion-corpuscles, or as products of coagulation. I am unable to see in these formations a structure different from that of cartilage-corpuscles or that of living protoplasm in general; true, in the ganglion-corpuscles the structure is very prominent. Such spokes are in some cases also distinctly seen to project from the periphery of the ganglionic cor-

N

V

t

FIG. 42.—SECTION FROM THE CORTEX OF THE BRAIN OF A RECENTLY KILLED GROWN RABBIT; KEPT IN A ONE-HALF PER CENT. SOLUTION OF CHLORIDE OF SODIUM. [PUBLISHED IN 1873.]

P, the grayish reticulum of living matter, with numerous nuclei, *N*. Magnified 800 diameters.

FIG. 43.—SPECIMEN FROM THE CORPORA QUADRIGEMINA OF A RECENTLY KILLED GROWN RABBIT; KEPT IN A DILUTE SOLUTION OF BICHROMATE OF POTASH. [PUBLISHED IN 1873.]

In the grayish reticulum of living matter there are nuclei, *N*, ganglion corpuscles, *G*; with axis-cylinder offshoots, *A*. Some axis-cylinders with varicosities, *V*. Magnified 800 diameters.

* The literature is found in Jul. Arnold, "Ein Beitrag zu der feineren Structur der Ganglienzellen." Virchow's Archiv, 41 Bd. 1867.

puscles, as well as to proceed from the medullated and non-medullated nerve-fibers, and to traverse the light rim around all these formations.

The same structure is visible in the ganglionic corpuscles of the sympathicus nerve of the rabbit. Here the spokes directly connect corpuscles lying near each other, and penetrate also the interstice between the corpuscles and the capsule, being lost to sight in the latter.

EF

MF

FIG. 44.—SURFACE-EPITHELIUM OF A VILLUS OF THE SMALL INTESTINE OF A GROWN DOG. SLIGHT GOLD STAIN. [PUBLISHED IN 1873.]

EL, columnar epithelia in side view; *EF*, columnar epithelia in top view; *ML*, epithelium transformed to mucus, in side view; *MF*, same in top view; *S*, the striated seam of the epithelia. Magnified 800 diameters.

The pale protoplasma of the nervous system, as is well known, is easily stained violet with solutions of chloride of gold, and such solutions, cautiously applied, furnish a valuable means more plainly to bring to view the features of the structure of nerve-elements described.

Epithelial Tissue. The forms of the so-called "prickle and ridge cells" are known in many epithelia; they have been first described by Max Schultze* as normal occurrences in the pavement epithelia of the skin, the lips, the mucosa of the oral cavity, the tongue, and the conjunctiva of the eyelids. The thorns are nothing but offshoots of an epithelial corpuscle, which traverse the light rim of cement-substance to join all the neighboring corpuscles. The thorns are conical. They are either so arranged that from one element alternately the broad base of a cone projects, and the next thorn is inserted with its point into the element; or, as Bizzozero has demonstrated, the points of the thorns projecting from two neighboring corpuscles meet in the rim of the cement-substance.

Owing to these offshoots, the cement-substance, if cautiously stained brown by nitrate of silver, is pierced by transverse light

* Centralblatt für die Mediz. Wissenschaften, 1864.

lines; whereas gold tinction colors the projections interconnecting the violet epithelial bodies also violet, leaving the cement-substance unstained.

I have not seen elements in epithelia other than so-called "prickle-cells" interconnected with one another. (See Figs. 44 and 45.)

From my descriptions it follows that all elements of the tissues of the animal body are "prickle-cells," all nuclei are "prickle-nuclei," and all nucleoli "prickle-nucleoli."

Examining the epithelial corpuscles of glands, we are satisfied that the projections of one "enchyma-cell" not only reach all neighboring "enchyma-cells," but that at the periphery of the lobule or tubule of a gland they establish a direct union between the enchyma and the connective-tissue corpuscles.

The first conclusion to be drawn from my researches is that in no tissue whatever do there exist "cells" as isolated individuals.

Each tissue represents, speaking in the usual way, a colony of cells, in which one cell is uninterruptedly united by filaments of living matter with all, and all with one. Each "cell-colony" again is connected with the neighboring colonies without interruption, so that the whole animal body may be considered as a single cell-colony. In other words:

A

C

FIG. 45.—SECTION OF THE SUBMAXILLARY GLAND OF A MIDDLE-SIZED RABBIT. SLIGHT GOLD STAIN. [PUBLISHED IN 1873.]

AA, acini lined by epithelia (termed also "enchyma-cells"). *C*, connective-tissue frame. Magnified 300 diameters.

The animal body, as a whole, is one protoplasmic mass, in which are imbedded a relatively small number of isolated protoplasmic corpuscles (migrating, colorless, and colored blood-corpuscles), *and various other non-living substances* (glue-yielding and mucous substances, fat, pigment-granules, etc.).

Just as the amœba is a protoplasmic lump, in which the living matter is arranged in the form of a reticulum, whose points of intersection are also living matter, so the body of even a highly organized mammal is a lump, traversed by a living reticulum, whose points of intersection are living matter in the shape of protoplasmic corpuscles, hitherto termed cells.

FIG. 46.—SCHEMA OF THE STRUCTURE OF THE VARIETIES OF CONNECTIVE TISSUE. [PUBLISHED IN 1873.]

Every tissue, as the history of development teaches, is buil up by a number of protoplasmic lumps, which we may consid as the *elements* of the tissue. In a completely formed tissue, th cell and its territory (Virchow) represent the *unit* of the tissu

which is by no means an individual, as each unit is in direct, living connection with all neighboring units.

Let us begin with the analysis of the units in the formations termed "connective tissue." In the center of the element is the nucleolus, around this the nucleus, and next a protoplasmic body, hitherto termed "cell"; this is surrounded by a protoplasmic mass, infiltrated with a glue-yielding basis-substance, and within this unit of the tissue the living matter is uninterruptedly connected. It is accumulated in the center in the shape of a compact *nucleolus;* next it constitutes a sometimes narrow, sometimes wide, reticulum, and incloses this reticulum as a continuous layer in the shape of the *nucleus;* then it forms a somewhat wider reticulum, holding protoplasmic liquid, and, as a rule again, a continuous shell, inclosing this reticulum in the shape of the *cell;* and, lastly, is spread out in the shape of a relatively wide reticulum, whose meshes are infiltrated with basis-substance, as the *cell-territory.* (See Fig. 46.)

This *schema* may exhibit modifications if either the nucleus *in toto* or the whole element *in toto* is a compact, homogeneous mass of living matter. Such conditions are due, as I have explained before (see page 46), to differences of age of the protoplasm.

Each of the constituents of a unit described is separated from the neighboring constituents by a space, as a rule, containing a liquid, traversed not by a reticulum, but simple filaments of the living matter. Such spaces, therefore, exist around the nucleolus, around the nucleus, around the protoplasm, or cell, and around the infiltrated portion of the unit, although until the present time only the pericellular spaces were known. In all these spaces a circulation of liquids can take place, and each may be filled by parenchymatous injection with colored substances. Such injections have been made around the nucleus (by Mac-Gillavry); around the cell (by Kowalewsky and others); around the borders of the units of the tissue, and, lastly, around the perivascular spaces. By such forcible injections the connecting filaments are torn and the protoplasmic bodies become displaced and compressed. We can readily understand how lymph-clefts, destitute of walls, could be manufactured by such parenchymatous injection.

The *schema* of the units of *epithelium* is different. In the center of the element is the nucleus with the nucleolus. Both are imbedded in a protoplasmic body surrounded by the shell of cement-substance common to all neighboring elements,

which contains the spokes or prickles connecting the elements. Features similar to those of epithelia may also be exhibited by some connective-tissue corpuscles, especially those of the medullary tissue (osteoblasts) and the endothelium; the same are found in the tissue of smooth muscle. I intend to demonstrate hereafter that the development of a unit of connective tissue is invariably preceded by a stage which corresponds to the *schema* of epithelial formation; we are therefore not justified in making an essential difference between the elements of connective tissue and those of epithelium, exclusively based on differences in their shape.

Just as each independent protoplasmic lump, and within it each vacuole, is bordered by a continuous layer of living matter, so the body of a mammal, and in its interior every cavity, is covered by a continuous layer of protoplasm.

Based upon the facts hereinbefore described, we may obtain, as I shall later show, a clear view of the development of the tissues and of the inflammatory process. During inflammation, especially that of certain tissues, conclusive proofs are furnished that there is in the basis-substance a large amount of living matter which is liable to become diseased.

Is Blood a Tissue? As one of the consequences of the modern views regarding individuals, it is held that blood, pus, secretions, etc., are fluid tissues. I have demonstrated that every animal tissue is a continuous mass of protoplasm, with zones of different structure. An "intercellular substance" exists here as little as "cells," in the modern sense, are present. We are justified in speaking only of *basis-substance*.

That single lumps, as *migrating cells*, discovered by Von Recklinghausen, are, for a time, disconnected from other elements and execute locomotion of their own, does not alter the general rule. Migrating corpuscles are not essential constituents of a tissue.

In the blood, isolated protoplasmic lumps, the red and colored blood-corpuscles, float in a liquid plasma. Protoplasmic lumps are likewise suspended in liquids such as pus, colostrum, bile, sperm, etc. Such liquids we have no right to call tissues.

The analogy between a living amœba and the body of a higher animal as to its living blood-corpuscles is apparent enough. In the amœba there arise transient vacuoles, in some of which, as I have demonstrated before (see page 22), granules

of the contractile matter may be suspended; and blood-vessels arise from the formation of vacuoles (see page 36), containing from their very origin a liquid in which isolated lumps of living matter are suspended.

RESEARCHES AND DEDUCTIONS SINCE 1873.

I have purposely given an accurate translation of my assertions in 1873, in order to show that the cell-theory and its consequences, in the light of my investigations, had to be abandoned. At present, after nine years' further research, I have nothing to alter in my previous statements, and but little to add.

Various publications, based on studies made in my laboratory during the last seven years by unprejudiced observers, fully corroborate the new views. Not only physiological and histological research, but pathological investigation as well, will become more fruitful. Inflammation, tuberculosis, formation of tumors—in short, all morbid processes—will be better understood than is possible with cellular-pathological views.

L. Elsberg, in 1875,* makes the following statements:

"Not only in the wide domain of organic physiology, but especially also in human pathology, the cell doctrine has been accepted so universally that it seems to me eminently proper to bring the new views to the notice of the American Medical Association, even at this early stage of their crystallization into a complete doctrine. All that I shall present to you as histological fact has been repeatedly observed and demonstrated by C. Heitzmann, both at Vienna and New York; and a number of others, as well as I, have been enabled to confirm his observations.

"The ideas of humoral and solidistic pathologists long continued to influence medical teachings after Schwann's discoveries of the elementary structure of tissues were generally acknowledged as correct, and more or less consistently applied. It was really not until Virchow promulgated his celebrated lectures on cellular pathology, less than twenty years ago,—lectures which reached and deeply impressed the medical profession in every portion of the globe,—that the cell-doctrine has had undisputed sway."

* Notice of the Bioplasson Doctrine. Transactions of the American Medical Association, 1875.

In Lecture I., delivered February 16, 1858, Virchow said: "If we consider the extraordinary influence which Bichat, in his time, exercised upon the state of medical opinion, it is indeed astonishing that such a relatively long period should have elapsed since Schwann made his great discoveries without the real importance of the new facts having been duly appreciated. This has certainly been essentially due to the great incompleteness of our knowledge with regard to the intimate structure of our tissues, which has continued to exist until quite recently, and, as we are sorry to be obliged to confess, still even now prevails with regard to many points of histology, to such a degree that we scarcely know in favor of what view to decide. Especial difficulty has been found in answering the question from what parts of the body action really proceeds, what parts are active, what passive; and yet it is already quite possible to come to a definite conclusion upon this point, even in the case of parts the structure of which is still disputed. The chief point in this application of histology to pathology is to obtain a recognition of the fact that the cell is really the ultimate morphological element in which there is any manifestation of life, and that we must not transfer the seat of real action to any point beyond the cell." And further on he said: "According to my ideas, this is the only possible starting-point of all biological doctrines. If a definite correspondence in elementary form pervades the whole series of all living things, and if in this series something else which might be placed in the stead of the cell be in vain sought for, then must every more highly developed organism, whether vegetable or animal, necessarily, above all, be regarded as a progressive total, made up of a larger or smaller number of similar and dissimilar cells. Just as a tree constitutes a mass arranged in a definite manner, in which, in every single part, in the leaves as in the root, in the trunk as in the blossom, cells are discovered to be the ultimate elements, so it is also with the forms of animal life. *Every animal presents itself as a sum of vital unities*, every one of which manifests all the characteristics of life. The characteristics and unity of life cannot be limited to any one particular spot in a highly developed organism (for example, to the brain of man), but are to be found only in the definite, constantly recurring, structure which every individual element displays. Hence it follows that the structural composition of a body of considerable size, a so-called individual, always represents a kind of social arrangement of parts, an arrangement of a social kind, in which a number of individual existences are mutually dependent, but in such a way that every element has its own special action, and even though it derive its stimulus to activity from other parts, yet alone effects the actual performance of its duties. I have therefore considered it necessary, and I believe you will derive benefit from the conception, to portion out the body into *cell-territories* (Zellen-territorien). I say territories, because we find in the organization of animals a peculiarity which in vegetables is scarcely at all to be witnessed, namely, the development of large masses of so-called *intercellular substance*. Whilst vegetable cells are usually in immediate contact with one another by their external secreted layers, although in such a manner that the old boundaries can still always be distinguished, we find in animal tissues that this species of arrangement is the more rare one. In the often very abundant mass of matter which lies between the cells *(intermediate, intercellular substance)* we are seldom able to perceive at a glance how far a given part of it belongs to one or another cell; it presents the aspect of a homogeneous intermediate substance. According to Schwann,

the intercellular substance was the cytoblastema destined for the development of new cells. This I do not consider to be correct, but, on the contrary, I have, by means of a series of pathological observations, arrived at the conclusion that the intercellular substance is dependent in a certain definite manner upon the cells, and that it is necessary to draw boundaries in it also, so that certain districts belong to one cell, and certain others to another. You will see how sharply these boundaries are defined by pathological processes, and how direct evidence is afforded that any given district of intercellular substance is ruled over by the cell which lies in the middle of it, and exercises influence upon the neighboring parts.

"It must now be evident to you, I think, what I understand by the territories of cells. But there are simple tissues which are composed entirely of cells, cell lying close to cell. In these there can be no difficulty with regard to the boundaries of the individual cells, yet it is necessary that I should call your attention to the fact that, in this case, too, every individual cell may run its own peculiar course, may undergo its own peculiar changes, without the fate of the cell lying next to it being necessarily linked with its own. In other tissues, on the contrary, in which we find intermediate substance, every cell, in addition to its own contents, has the superintendence of a certain quantity of matter external to it, and this shares in its changes—nay, is frequently affected even earlier than the interior of the cell, which is rendered more secure by its situation than the external intercellular matter.

"Finally, there is a third series of tissues, in which the elements are more intimately connected with one another. A stellate cell, for example, may anastomose with a similar one, and in this way a reticular arrangement may be produced similar to that which we see in capillary vessels and other analogous structures. In this case it might be supposed that the whole series was ruled by something which lay, who knows how far off; but upon more accurate investigation, it turns out that even in this chain-work of cells a certain independence of the individual members prevails, and that this independence evinces itself by single cells undergoing, in consequence of certain external or internal influences, certain changes confined to their own limits, and not necessarily participated in by the cells immediately adjoining." *

"Now, according to Heitzmann, what Virchow asserts of 'a third series of tissues' is really true of all tissues. Not only are there contained no cells as isolated individuals in any tissue of the body, but no tissue in the body is isolated from the others. He prefers not to use the term 'cells'; he speaks of 'living matter,' and this he asserts is continuous throughout the whole body. If we desire to retain the use of the word cell to designate the living-tissue elements, we must regard each cell to contain a net-work of living matter within it, and every cell connected by threads of living matter with every other cell in its neighborhood. . . .

* "Cellular Pathology, as based upon Physiological and Pathological Histology." By Rudolf Virchow. Translated from the second edition by Frank Chance, B. A., M. B., Cantab., etc. New York: Robert M. DeWitt. Pp. 29, 40, et seq.

"Allow me to impress this fact upon you, that these are things which each and every one of you can see for himself if he only has a good microscope, good eyes, and an *unprejudiced mind.* Don't look for any so-called 'cells,' and don't imagine, as I used to do, that it is given to only a favored few to be able to penetrate these mysteries of nature. The only danger is that you become so much fascinated with histological investigations as to neglect other important things.

"It is the merit of Heitzmann to have discovered, in the first place, that the living matter in its simple form, as seen in an amœba, the so-called basis-matter of life, to which hitherto the name of protoplasma has been applied, but which I propose to designate as bioplasson, is not without structure, as has before his accurate investigations been supposed, and that its structure is that of a net-work, in the meshes of which the bioplasson fluid, or the not contractile, not living portion of the organism exists. He discovered that the granules, which had been observed before, are not foreign or accidental occurrences, but that they are part and parcel of the living matter—that, in fact, they are the thickened points of intersection of the threads of bioplasson constituting the living net-work. Extending his investigations, he found that what was true of the structure of bioplasson in the amœba, where a single unit-mass of living matter constitutes the entire individual, is true of the structure of bioplasson of all, even the highest, living organisms. The idea connected with the word *cell*, when this term was first applied to the organic form element, had, with the advance of microscopical and histological knowledge, gradually undergone such changes that the name had become a complete misnomer. Although 'cells' were still spoken of, it was understood that their essential constituent was living matter individualized into small, distinct masses. The existence in these of a nucleus, a nucleolus, even a nucleolinus and granules, was known; even thorns and processes had been observed occasionally. But all this knowledge of the structure of these elementary masses was fragmentary, until Heitzmann announced that the nucleus, nucleolus, granules, and threads are really the living contractile matter; that it is arranged in a net-work containing in its meshes the non-contractile matter which is transformed into the various kinds of matrix characterizing different tissues; and that the tissue unit-masses of bioplasson throughout the whole body are interconnected with fine threads of the same living matter.

"On the significance of these discoveries, and their bearing upon the question of physiology and pathology, I can here say but a few words. The more our knowledge of the minute anatomy, or rather morphology, of the organism advances, the more explicable becomes the functional activity of the various parts and tissues. So long as the cell was looked upon as the simplest form element of the body, we could not hope to go beyond the cells, and their performances in health and disease. Unfortunately, their investigation could not explain essential vital phenomena, the real activity of living matter. To-day we have it in our power to examine almost all tissues of the animal body while they are alive, by preventing, in thin sections placed under the microscope, evaporation or drying upon the one hand, and by supplying, on the other, such artificial temperature and other conditions as are necessary for the vital manifestation of the particular tissue under investigation. And, enabled directly to observe the phenomena which accompany movement of living matter, its contraction, we may hope to attain clear conceptions of the mysterious activity of muscles, of nerves, even of epithelia, which form secretory organs. I may instance Heitzmann's discovery of the manner in which primary muscle-bundles are constituted, as showing how easy it is to understand the observed phenomena of muscular contraction and innervation, if we have correct information as to the morphological arrangement. Without going into the details, I may say that a primary bundle is made up of rows of sarcous elements and muscle fluid, the former united by threads of living matter, as mentioned before. Contraction of the whole muscle consists in this: that the sarcous elements become larger, and the threads shorter. Kühne has shown that the motor nerve does not enter the muscle fiber, but ends knob-like at its side, in about the middle; here the contraction commences, and proceeds toward each end. In fact, we find everywhere that definite physiological functions depend upon definite morphological arrangements, and we may well make deductions from the latter as to the former.

"Pathology will doubtless derive much advantage from the bioplasson doctrine. We are enabled to observe quantitative and qualitative changes of living matter in the smallest constituents of the body. We know that the disposition of living matter is different in different persons, and that, in the case of increased supply of food, the reaction is different in strong and healthy people on the one hand, and the sick and weak on the

other. Indeed, upon this knowledge rests, to-day, the whole doctrine of tuberculosis. It may be that we shall yet learn to know the differences in the behavior of living matter toward different re-agents, or differences in its quantitative arrangement, so that we may, perhaps, become able, from the examination of a few colorless blood-corpuscles, to gain an insight into the condition and vital power of the whole individual. If this comes to pass, it will be possible to recognize certain diseases by means of the microscope before they are sufficiently developed to do much harm; and we may thus come a step nearer to the highest aim of the physician—the prevention of disease. At all events, every exact scientific investigation, even though at first of theoretical value only, sooner or later brings with it some practical benefit."

The hopes here expressed have already, to a certain degree, been realized, and the practical value of the new discoveries demonstrated.

In 1879, I said in the introduction of an essay: *

"I am far from blaming any physician who, perhaps ten or even five years ago, has studied microscopy, and left it disgusted or in despair. The standard doctrine of 'cells' and the 'cellular pathology' was unsatisfactory indeed. Beyond the proof of the presence of cells, microscopy did not advance, and the examiners have been satisfied if they could see cells, the greatly varying shape and size and appearance of which they had to admit, without knowing any of the causes of the variations.

"To-day the cell-doctrine is surpassed by new discoveries. Instead of looking at the shape of the cell, we have learned to study the minute structure of its mass, the so-called protoplasm, of which we know that it represents a constituent part of the organism. Many of the morbid relations of the protoplasm have been revealed, and made use of for practical purposes. We climb upward upon the shoulders of the ingenious founder of the cellular pathology, R. Virchow; and that the new doctrine, for which has been proposed the term 'bioplasson-doctrine,' has really arrived at a certain point of perfection, I presently intend to demonstrate."

For the researches and deductions here alluded to, see page 58.

* "The Aid which Medical Diagnosis receives from Recent Discoveries in Microscopy." Archives of Medicine, 1879.

The re-agents which I used in 1873, with predilection, viz., the nitrate of silver and chloride of gold, are not always reliable, and I admit, had my assertions been based exclusively on specimens treated with these re-agents, they would justly have been considered as nearly worthless. Besides, a certain amount of skill in using those re-agents, and a well-trained eye, are required to see what really can be seen. This is evidently the reason why in Europe, of the many investigators who tried to bring to view the connections of cartilage-corpuscles after 1872, when I first found these connections, only very few have succeeded. Still it was absolutely necessary to demonstrate the presence of such connections, because on cartilage-tissue have mainly rested, for the last forty years, our biological views.

A. Spina* deserves great credit for the discovery of a new method, by which the connections of cartilage-corpuscles become readily demonstrable even to a relatively untrained eye. This method is as follows: the cartilage, best from the articular ends of bone, for three or four days is placed in alcohol, cut and examined in alcohol. "We are satisfied," Spina says, "that from the cells of the hyaline cartilage project solid offshoots; these, as is easily seen, arise from the bodies of the shriveled cells, pervade the basis-substance, and blend with the offshoots of other cells. The thickness and number of the offshoots greatly vary; the most numerous and most delicate were found in specimens from the superficial portion of articular cartilages of middle-sized frogs," etc., etc.

From what I have seen, I can heartily recommend this method for the demonstration of the connections, though it is, on account of the shrinkage due to the preservation in alcohol, imperfect. This method brings to view, also, the delicate, mostly rectangular reticulum in the basis-substance of fibrous connective-tissue formations, adjacent to cartilage.

S. Stricker† recently makes the following statements:

"The so-called migrating cells in the substantia propria of the cornea, so far as can be ascertained by direct, continuous observation, are neither migrating nor isolated cells. We can easily see, under suitable conditions, that portions of their bodies gradually assume the looks of basis-substance, while new

* "Ueber die Saftbahnen des hyalinen Knorpels." Sitzungsber. d. Wiener Akad. der Wissensch., 1879.

† "Mittheilung über Zellen und Grundsubstancen." Wiener Mediz. Jahrbücher, 1880.

additions to the cell-body are formed from the neighboring basis-substance.

"The basis-substance, under favorable conditions, exhibits in its interior form-changes like those of amœboid cells. A net-like arrangement, fibrillæ, and other forms, come and go. The basis-substance and the migrating cells in it represent a continuous mass, which, according to circumstances, may assume the features of basis-substance or of wandering cells. A lump of this mass becomes a real migrating cell only if separated from its surroundings, which, however, does not occur in the continuity of the substantia propria.

"The epithelia of the cornea, with their so-called cement-ledges, likewise form a continuous living mass. Under favorable conditions, we can easily realize that neither the cement-ledges nor the cells are stable formations. The cement-ledges are transformed into constituent parts of the neighboring cells, while within the cells new cement-ledges arise, so that after a while the configuration of the epithelium has changed, or else the whole form of the cells of the anterior epithelium is lost to sight, and it appears as a uniform mass, such as is the rule in the normal living cornea.

"Changes of the branching cells in the substantia propria are easily seen during the first few minutes after excision of the cornea, by suitable methods of preparation.

"The interior of the cell-bodies undergoes manifold visible variations. One of the most remarkable instances is furnished by the saliva-corpuscles. The assumption that a so-called molecular motion takes place in the saliva-corpuscles, is erroneous. The granules seen with insufficient amplifications are transverse sections of trabeculæ. The saliva-corpuscle is traversed by a sharply marked trabecular structure (Balkenwerk), which, so long as the corpuscle is fresh, executes lively wavy motions. The waving gradually ceases on the addition of solutions of salts in certain concentration, and the reticular structure disappears. The waving is now replaced by very slow form-changes in the interior mass."

VII.

CONNECTIVE TISSUE.

Definition and Division.

THE term *connective tissue* is applied to that tissue which constitutes the frame of the body (skeleton), covers the articular surfaces of bones (articular cartilage), incloses the whole body (derma of skin), supports and surrounds muscles and nerves (tendon, perimysium, perineurium), produces flat layers for all epithelial formations (basement layers), contains as a physiological product fat-globules (fat-tissue), and forms the blood and lymph vessels. It is composed of living matter which, having a reticular structure, contains in its meshes a lifeless, more or less solid, interstitial basis-substance. At certain regular intervals the reticulum is nodulated, and these nodules are the formerly so-called connective-tissue cells, preferably termed connective-tissue corpuscles.

The distinguishing feature of connective tissue is the *interstitial basis-substance,* which is generally termed "glue-yielding," because some of its varieties on being boiled furnish gelatine, although other varieties, by the same treatment, yield a substance which is not strictly glue, but kindred to it. For twenty years (1840–1860) a lively controversy was carried on regarding the relation between the basis or intercellular substance and the plastids, the connective-tissue cells. Henle was the main representative of the view that the intercellular substance contains only

cavities, while Virchow asserted that the intercellular substance contains "cells," the seats of life. Between 1860 and 1870, histologists began to be aware that the intercellular substance contains cavities, in which the cells are imbedded. Virchow, in 1851, was also the first to recognize that all varieties of connective tissue belong to one group, for the designation of which he proposed the rather unsatisfying term "connective substances."

As A. Rollett * says: "The connective tissues are developed from the middle germinal layer, in which blood and muscle also originate. The typical connective substances are recognized histologically by the circumstance that they contain extensive and continuous layers of material (intercellular substance), which, when compared with the cellular structures distributed through its substance (protoplasma), or the morphological elements in other tissues, always appears as a more passive substance and one which participates but slightly in the processes characteristic of life. These masses consist, for the most part, of gelatine-forming substances, such as collagen, chondrogen, and ossein. The connective tissues frequently pass by substitution or genetic succession into one another; they appear, therefore, to be morphologically equivalent, so that in many instances certain organs, or parts of organs, belonging to animals nearly allied to one another, are formed sometimes of one, sometimes of another, of these tissues."

The basis-substance, the hitherto called intercellular substance, is a product of the lifeless bioplasson liquid which, probably nitrogenous from the very beginning, is transformed by chemical changes into the nitrogenous, more or less solid, mass termed basis-substance. In the same variety of connective tissue, especially in the fibrous, the basis-substance may exhibit different degrees of solidification. Bundles of fibrous connective tissue are, f. i., built up of striated, glue-yielding *basis-substance;* the bundles are separated from each other by the less solid *cement-substance;* and they are bounded, both at their peripheries and around the plastids, by a more solid, dense, and chemically indifferent *elastic substance.* The so-called elastic fibers are but a variety of the glue-yielding basis-substance, in a high degree of solidification.

According to the nature of the interstitial substance, the morphological properties of which are far better known than the chemical, we may distinguish four varieties:

Myxomatous or mucoid basis-substance, a jelly-like, translucent substance, not yielding gelatine;

* "A Manual of Histology," by S. Stricker. American translation edited by Albert H. Buck, 1872. Chapter: "The Connective Tissues."

Fibrous basis-substance, a semi-solid, opaque substance, characterized by a striated, fibrous, or lamellated appearance, yielding, on being boiled, glue or a substance kindred to glue;

Cartilaginous or chondrogenous basis-substance, a dense, opaque substance of a uniform hyaline or striated appearance, which on being boiled also yields a liquid kindred to glue, as indicated by its odor; and

Osseous or bony basis-substance, a dense, opaque, glue-yielding substance, of a striated or lamellated appearance, infiltrated with lime-salts.

The character of any variety of connective tissue is exclusively defined by the character of its basis-substance, whereas the connective-tissue corpuscles, though greatly varying in size and shape, are all essentially the same, viz.: living matter hitherto called "protoplasm." These protoplasmic bodies, plastids, as a rule nucleated, lie in cavities of the basis-substance, representing what has been termed the "fixed cells" of connective tissue. Besides, in some varieties of connective tissue, plastids are met with which, under favorable conditions, exhibit rapid changes of shape and locomotion. Von Recklinghausen* first drew attention to the presence of these "migrating cells." Such corpuscles can change their location only in the interstitial liquid portions of the basis-substance. Their presence is by no means the rule.

Of the connective-tissue corpuscles, of course the "fixed cells" alone are united with each other. In myxomatous tissue the corpuscles are connected by thick and wide offshoots, constituting the "stellate cells" of Virchow. In hyaline cartilage the union is by delicate offshoots; while in the fibrous tissue, in fibrous cartilage and bone, the corpuscles are joined by both thick and slender offshoots. The basis-substance, which was formerly supposed to be structureless, is to-day known to be traversed by a delicate reticulum of living matter, the meshes of which are somewhat larger than that of the plastids; by means of this reticulum the connection between the plastids is established.

The reason why the reticular structure of the basis-substance is not, or so little, marked in the fresh condition of the tissue, is that there is not sufficient difference between the refracting power of basis-substance and of living matter. It can be brought to view either by staining re-agents, such as nitrate of silver and chloride of gold, or by alteration of the refraction of the basis-substance, such as its liquefaction in the inflammatory process or deposition of lime-salts. The latter occurrence, both in normal and morbid

* Virchow's Archiv. Bd. xxviii.

conditions, is an excellent means to render the reticulum in the basis-substance of cartilage visible, without any re-agent. In ground specimens of dry bone the cavities (lacunæ) and their offshoots (the canaliculi) are very marked, especially if filled with air or other extraneous matter, because the difference in the refraction of the calcified basis-substance and the cavities, deprived of their bioplasson, is very great. The more the lime-salts are extracted from the basis-substance — f. i., by a solution of chromic acid, which at the same time preserves the bioplasson — the less visible are the cavities and their offshoots. A small amount of lime-salts, left behind even after chromic-acid treatment, renders both cavities and canaliculi, both the bone-corpuscles and their offshoots, plainly visible.

The development of basis-substance invariably takes place from the bioplasson liquid. Either single plastids are infiltrated with basis-substance and rendered pale, apparently structureless, or the process takes place in a number of coalesced plastids, from which the formation of a territory results. Within this territory unchanged plastids are left, the connective-tissue corpuscles proper. The first manner of formation of basis-substance occurs in the simplest and earliest varieties of myxomatous connective tissue, the latter manner in all higher developed forms of fibrous, cartilaginous, and bony connective tissue.

(1) *Myxomatous or Mucoid Tissue.* Myxomatous tissue is the earliest connective-tissue formation in the embryo, and all later varieties of connective tissue arise from this. As soon as the mesoblast is produced, we recognize it by the presence of numerous plastids, uniform in size and shape, some homogeneous, others granular and nucleated. All are connected by means of delicate filaments, traversing the light rim around each plastid. This tissue is called the *embryonal* or *indifferent tissue*, the latter term meaning that no difference can be discovered in the character of the plastids.

During the first few weeks of embryonal life we meet with myxomatous connective tissue only, and also during the entire period of intra-uterine development this kind of tissue largely prevails; it also forms the tissues destined for the attachment of the embryo to the womb and for its nutrition, viz.: the placenta and the umbilical cord. With advancing development of the body the myxomatous tissue is replaced by more advanced formations, and in the full-grown individual only the vitreous body of the eye exhibits features similar to those of the umbilical cord (Virchow). We also meet with it in all remnants of embryonal development, such as medulla of bone, adenoid or lymph-tissue (lymph-ganglia, spleen, submucous adenoid layers), and tooth-pulp.

In the animal organism, myxomatous tissue appears in the following varieties:

(a) Medullary Tissue, found in medulla of bone at an early stage of development. The human embryo exhibits this tissue in the first few weeks. Plastids, either solid, or granular and nucleated, globular or spindle-shaped, and of varying size, are scattered in a scanty jelly-like basis-substance. This substance, examined without any re-agent, looks granular with lower powers of the microscope, but with high powers exhibits a delicate reticulum, which blends with the delicate, thread-like offshoots from the plastids. Each field of the basis-substance corresponds in size and shape to one plastid or to a small group of plastids; the earliest formations of basis-substance arise from single plastids, by a chemical alteration of the bioplasson liquid, without the formation of territories. (See Fig. 47.)

C.

FIG. 47.—MEDULLARY TISSUE OF CHEST OF HUMAN EMBRYO, FOUR WEEKS OLD.

C, medullary tissue, probably tending toward the formation of cartilage of ribs; *P*, medullary tissue, probably tending toward the formation of fibrous perichondrium. Magnified 600 diameters.

The medulla of bone exhibits this variety of myxomatous tissue at the fourth and fifth month of embryonal life of man, and in the case of pup or kitten at the corresponding stage, viz.: time of birth.

Fig. 33 represents this tissue in a chromic-acid specimen; Fig. 34, stained with chloride of gold, in order to demonstrate the structure of the basis-substance.

The plastids in medullary tissue often assume the spindle shape, and here, too, we are satisfied that every field of basis-substance arose from an original plastid, without formation of territories. The embryonal and the medullary tissue in both varieties are prototypes of tumors, termed "round-cell and spindle-cell sarcoma" (globo and spindle myeloma). (See Fig. 48.)

(b) Reticular Tissue. This is the next stage in the development of myxomatous connective tissue. It consists of a reticulum of

either plastids or fibers, with nuclei at their points of intersection, inclosing a jelly-like basis-substance. The center of a field of basis-substance often contains a nucleus, which indicates that the field has originated from a plastid, the peripheral portion of which, by a chemical change of its liquid, was transformed into basis-substance, while the nucleus remained unchanged.

The placenta is, to a great extent, composed of this tissue, the reticulum being of a fibrous character, while distinctly nucleated plastids, the so-called "decidua-cells," fill the mesh-spaces of the reticulum.

The villi of the placenta consist of a reticulum of plastids with thickenings at the points of intersection, in close connection

FIG. 48.—MEDULLARY TISSUE OF BONE FROM THE SCAPULA OF A NEW-BORN KITTEN.

B, bone-tissue; *S*, myxomatous tissue composed of spindle-shaped plastids, traversed by a capillary blood-vessel. Magnified 800 diameters.

with the endothelial wall of the capillaries. Most of the mesh-spaces exhibit central nuclei. (See Fig. 49.)

The tissues of the body, which after more advanced development show the structure of fibrous connective tissue, are originally reticular. In many instances we encounter in very young embryos spaces, inclosed by a fibrous or plastid reticulum, which contain a jelly-like basis-substance, too large for admitting them to have originated from a single plastid. In some other instances

of reticular tissue no doubt a single plastid has become basis-substance, but here two or more plastids must have coalesced in order to produce a nucleated field of basis-substance—the first evidence of a territory. Formations of both these varieties, however, may occur in one and the same specimen. (See Fig. 50.)

FIG. 49.—RETICULAR MYXOMATOUS TISSUE OF A VILLUS OF THE PLACENTA OF A HUMAN EMBRYO, FOUR MONTHS OLD.

EE, epithelial cover of the villus, *B*, solid bud of a growing villus; *CC*, capillary blood-vessels, overlapped by the myxomatous reticulum. Magnified 500 diameters.

The lymph-ganglia, including the thymus of embryos and the spleen during the whole of life, exhibit the reticular myxomatous structure in a marked manner. (See Fig. 31.) The reticulum is either fibrous or composed of nucleated branching plastids,* while the meshes, varying greatly in size, contain plastids, either single or in groups, in all stages of development: the lymph-corpuscles. Of this variety of lymph-tissue the substance of the thyroid body may perhaps consist, although the spaces holding the lymph-

* C. Toldt has demonstrated that in the thymus of low vertebrates (frog, newt) the reticulum retains its protoplasmic character for life. Lehrbuch der Gewebelehre, 1877.

corpuscles in that substance are closed alveoli, and the walls of the alveoli are distinctly fibrous in character.

The reticular myxomatous tissue of the lymph-ganglia is the prototype of tumors termed Myxo-Sarcoma (Myxo-Myeloma). The more advanced tissue of the character of the thyroid body is found in all formations called lymph-adenoma. Some histologists claim that the connective tissue which surrounds the epithelial formations in the kidneys, in the salivary glands, and the connective tissue in the central nervous system, are reticular in structure. M. Schultze found this structure in the retina.

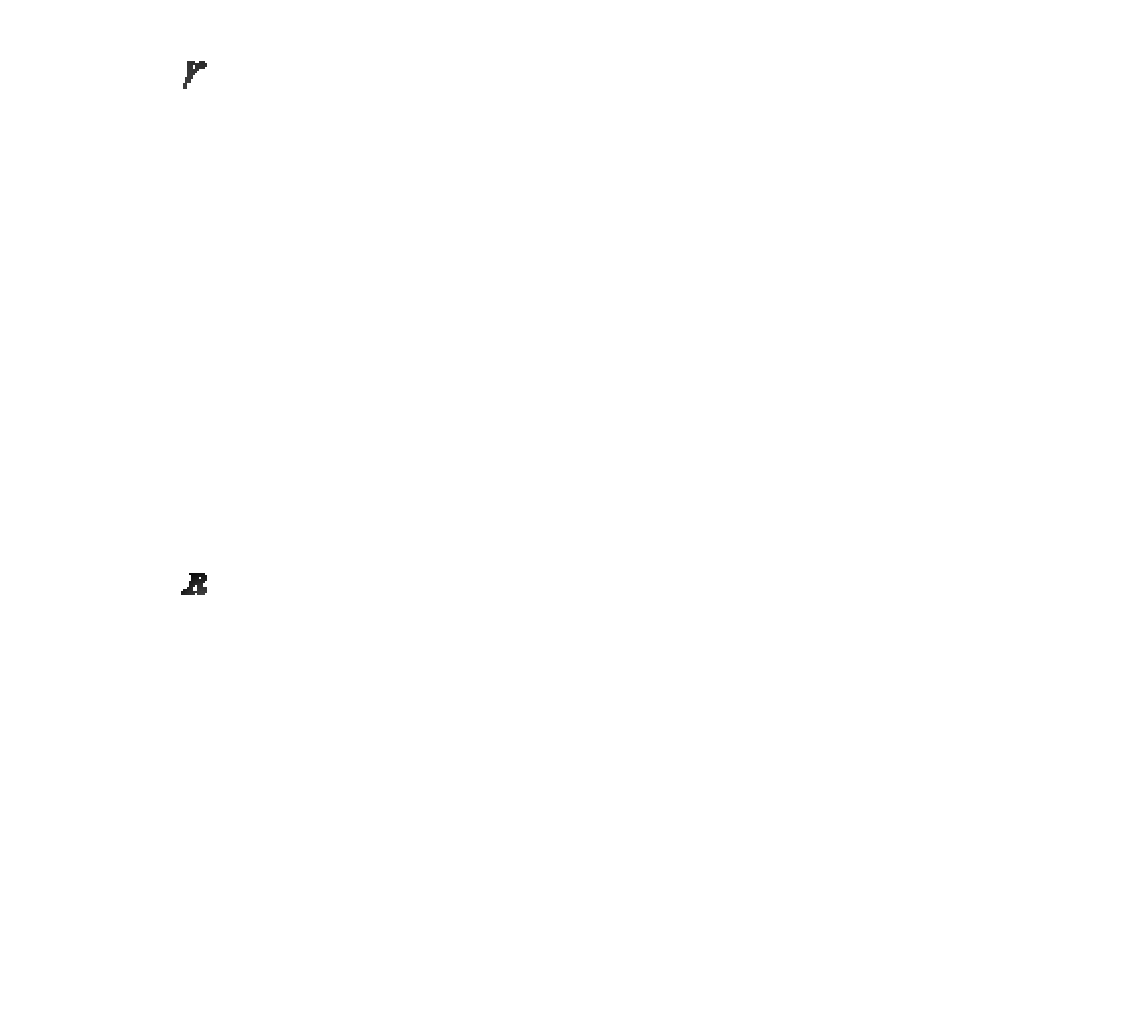


FIG. 50.—RETICULAR MYXOMATOUS TISSUE OF THE MUSCLE-FASCIA OF A HUMAN EMBRYO, TWO MONTHS OLD.

R, reticulum of plastids, or fibers with oblong nuclei at the points of intersection; *M*, striped muscle at an early stage of formation; *C*, capillary blood-vessel; *V*, vein. Magnified 500 diameters.

(c) Myxomatous Tissue of the Umbilical Cord. Virchow discovered in 1851 that the umbilical cord, formerly considered as a gelatinous formation (Wharton's jelly), is a regular mucoid tissue, traversed by a delicate reticulum of branching cells, in the meshes

of which is deposited the jelly-like "intercellular" substance. In this substance globular and isolated cells occur. Virchow found that, besides the three main blood-vessels (two arteries carrying venous blood, and one vein carrying arterial blood), there are no other vessels throughout the entire length of the umbilical cord. Capillaries exist only at a short distance (about one-half inch) close above the insertion of the cord into the abdominal wall. Virchow draws attention to the heavy coats of the vessels, the muscular character of which was discovered afterward by Kölliker, and concludes that these coats play an important part in the occlusion of the vessels whenever they are severed or torn,

V

V

FIG. 51.—SEGMENT OF THE UMBILICAL CORD OF A HUMAN EMBRYO, FOUR MONTHS OLD, IN TRANSVERSE SECTION.

A, artery, *V*, vein; *M*, myxomatous tissue, the common adventitia; *E*, epithelial cover. Magnified 25 diameters.

without ligature. The mucous tissue, Virchow * says, is attached to the imperfectly developed adventitial coat of the three vessels.

In my conception the umbilical cord *in toto* is the adventitial coat, common to the three blood-vessels, of which the vein, as a rule, has a much narrower muscle-coat than the two arteries. (See Fig. 51.) No capillary blood-vessels and no lymphatics have been discovered in this tissue, neither is anything certain in regard to nerves, though it is probable that the three vessels are

* "Die Cellularpathologie." Vierte Auflage. Berlin, 1871.

under the control of vasomotor nerves. The myxomatous tissue is often found to contain spaces, greatly varying in size and number, filled with liquid; these, doubtless, are secondary formations, so-called cysts. The outer surface of the umbilical cord is covered by a single layer of flat epithelia.

Now, if we compare a transverse section of the umbilical cord with an amœba (see page 21), the similarity between the two becomes evident. The epithelial coat of the cord corresponds to the continuous layer of living matter in amœba; the complex reticulum of plastids corresponds to the simple reticulum of living matter in the amœba; the closed cavities of the blood-vessels holding isolated plastids, the blood-corpuscles of the cord, correspond to the closed spaces, the vacuoles containing isolated granules of living matter. In fact, the simple amœba is the representative of the complex structure of the umbilical cord, as well as of all other tissues of the human body.

P

FIG. 52.—UMBILICAL CORD OF A HUMAN FŒTUS, NINE MONTHS OLD. CHROMIC ACID SPECIMEN.

P, bioplasson cords with nuclei at their points of intersection; *B*, partly homogeneous, partly fibrous, basis-substance. Magnified 500 diameters.

With lower powers of the microscope we recognize in sections of the umbilical cord of a fully developed human fœtus, both fresh and preserved and hardened in a chromic acid solution, a relatively coarse reticulum of plastids, Virchow's branching cells. The best sections are obtained from the portion about midway between the vessels and the surface, because nearer the vessels and the surface the reticulum, being very dense, does not admit of distinct demonstration. We see ramifying so-called protoplasmic strings of a delicate granular structure, containing oblong nuclei

usually at the points of intersection.* In the meshes the basis-substance is in part homogeneous, in part traversed by delicate fibrillæ. Not infrequently a nucleated string passes directly into a bundle of fibrillæ. In the center of a mesh-space we encounter sometimes a globular plastid, apparently isolated—*i. e.*, unattached to the strings forming the reticulum. (See Fig. 52.)

If we rub a stick of nitrate of silver over the surface of a piece of a fresh umbilical cord, it will soon become brown on exposure to daylight. Sections from such an umbilical cord will show light, branching spaces in a dark brown basis-

FIG. 53.—UMBILICAL CORD OF A HUMAN FŒTUS, NINE MONTHS OLD. STAINED WITH NITRATE OF SILVER.

S, light spaces, corresponding to the bioplasson cords in Fig. 52, branching and anastomosing, B, dark brown basis-substance, indistinctly striated and granular. Magnified [illegible] diameters.

substance. The light spaces correspond in size and shape to the strings seen in specimens preserved in chromic acid. They anastomose, and some of them send into the basis-substance smaller branches, which often divide and subdivide so much as to show a delicate, pencil-like appearance. The contours of the light spaces and their branches are in many places serrated. The brown

* In the umbilical cord of the pig-fœtus the nuclei of the cord are much more numerous than in the human.

basis-substance appears indistinctly striated and granular. (See Fig. 53.)

If we expose a piece of the fresh umbilical cord for some hours to the action of a large quantity of a one-half per cent. solution of chloride of gold, the specimen assumes in the daylight a dark violet color. Sections exhibit branching and connecting strings of dark violet color, whose nuclei at the points of intersection are either black or pale violet, while the basis-substance is but faintly stained either pale violet or pink. The strings in their general features and size correspond both to those seen in specimens preserved in chromic acid and to the light spaces found in specimens stained with silver. The pale basis-substance

Fig. 54.—Umbilical Cord of a Human Fœtus, Nine Months Old. Stained with Chloride of Gold.

P, dark violet bioplasson cords, corresponding to those in Fig. 52, and to the light spaces in Fig. 53; *B*, pale pink basis-substance, indistinctly striated. Magnified 500 diameters.

exhibits an indistinct striation, and some smaller offshoots from the violet strings pass into and are lost in striated bundles. (See Fig. 54.)

By comparing the chromic-acid, the silver-stained, and the gold-stained specimens, it is apparent that the light spaces are identical with the violet tracts, and these again identical with the bioplasson strings of the unstained specimen. In other

words, the nitrate of silver has stained the myxomatous basis-substance, and left the strings unstained, whereas the gold has stained the strings very much, the basis-substance, on the contrary, very little.

These facts convince us that Von Recklinghausen's theory, that lymph-spaces traverse the basis-substance and contain cells, is erroneous. The spaces produced by silver stain are not lymph-spaces, but bioplasson spaces, viz.: they are the bioplasson itself, unstained, or the cavities containing the unstained bioplasson. Unquestionably, such light spaces in silver specimens of various other tissues anastomose with the light spaces of the lymphatics, as bioplasson formations (plastids) are directly attached to the walls of the latter, and neither are stained by nitrate of silver. For further details of the minute structure of the umbilical cord I refer the reader to page 120, and to Fig. 35 and Fig. 36.

The *development of the myxomatous tissue* of the umbilical cord has not as yet been sufficiently studied for any positive statement. Of the minute structure of the vitreous body very little is known. From what I have seen in gold-stained specimens, and in the changes that occur on the borders of tumors of the choroid growing into the vitreous, I am convinced that the plastids of the vitreous body, most numerous at its peripheral portions, send delicate offshoots of living matter into the myxomatous basis-substance, which is alive throughout and liable to active morbid changes.

The *myxomatous tissue of the pulp of the tooth* will be dwelt upon in the chapter treating of teeth.

Fat-tissue. Our knowledge of fat-tissue is very limited. The main facts are as follows:

Fat-granules may arise from any bioplasson granule in isolated plastids and in plastids producing tissues of any description. The granules of living matter assume a higher degree of luster and increase slightly in size whenever they are about to change into fat-granules. As I have observed in colostrum corpuscles, the fat-granule at first remains connected by delicate filaments with the rest of the reticulum, and S. Stricker has observed that on the heating-stage fat-granules are expelled from a colostrum corpuscle. (See page 28.)

The chemical change by which the nitrogenous substances are converted into fat is not understood. It is even possible, according to a suggestion of L. Elsberg, that the plastidules are not directly transformed into molecules of fat, but are only mixed with them, so that in early stages of development of fat,

the plastidules may, by a retrograde metamorphosis, be reëstablished in their original structure.*

The fat-tissue met with in other varieties of connective tissue, chiefly the fibrous, consists of a number of fat-globules, aggregated into groups, which are termed fat-lobules. Such formations are seen, in greatly varying amount, in the subcutaneous tissue, the female breast, the omentum, and around the heart and the kidneys. The lobules being freely supplied with capillary blood-vessels, besides these contain only a small amount of a delicate fibrous connective tissue between the fat-globules.

Fat-globules, which vary greatly in size, are inclosed by a delicate continuous layer, termed the capsule of the globule. In this capsule there is almost invariably found an oblong, nucleus-like body, which in edge view appears to be fusiform, and blends with the capsule. The fat substance proper contained in the capsule is semi-fluid, and can be pressed out on artificially rupturing the capsule. Alcohol renders the fat coarsely granular, and causes it to shrink. Chromic acid solution, after a certain length of time, produces vacuoles in the fat-globule. Turpentine and oil of cloves dissolve the fat, and the nucleated capsule becomes plainly visible after the application of these re-agents.

In fat-globules preserved for a period of several months in a one-half per cent. solution of chromic acid, J. A. Rockwell, in my laboratory, discovered bioplasson masses in the middle of the fat. These masses, as a rule, appear coarsely granular with lower powers of the microscope, often branch, and sometimes contain a central nucleus-like body. High amplifications show that the granules and the nucleus are interconnected by means of delicate filaments. It also occurs that the bioplasson formation is flattened out near the capsule, or its granules are scattered at greater distances through a portion of the fat. Small globules contain one such granular formation, while large globules may hold two or more in addition to a varying number of scattered

* According to L. Ranvier ("Des Lésions du Tissu Cellulaire lâche dans l'Œdème," Comptes Rendus, 1871), in œdema produced by ligation of the vena cava and discision of one sciatic nerve of dogs, the connective tissue infiltrated with serum, twenty-four hours after the beginning of the œdema, shows cells, the peripheral protoplasma of which contains granules of a fatty appearance. Their refracting power is lower than that of fat, but if treated with a weak solution of chromic acid or bichromate of potassa, they become more highly refracting and smaller. These peripheral granules seem to be composed, he says, of fat and an albuminous substance, just as in the developing fat-cells.

granules. The granules are, in most instances, of a dim, gray color, and readily distinguished from the surrounding yellow fat. These formations are evidently those long known in specimens obtained from emaciated persons, and preserved in alcohol, as the nucleated, stellate protoplasmic bodies within the capsule. The intra-capsular protoplasm, according to C. Toldt,* retains its vital contractility even in the highest degrees of emaciation, and from it starts, under favorable conditions, the formation of new fat.

Fat-globules often contain a coloring matter, either diffused or in the form of pigment-granules; and even in the fresh condition they may contain needle-like formations, usually termed margaric acid crystals. More recent chemical researches show that these crystals are much more complicated formations of fat-acids than was thought formerly. Such crystals are frequently seen in rancid fat, where they produce large, dark clusters of radiating needles, standing out like the bristles of a porcupine.

Fat-globules originate from indifferent or embryonal plastids, which are considered by C. Toldt to be specific fat-formers. At first small granules of fat appear, which by coalescence produce globules. It has been maintained that each plastid will furnish a complete fat-globule, often of large size; whereas the researches of Flemming, Czajewicz, and others make it highly probable that a number of plastids are fused together in order to produce a large fat-globule. Flemming drew attention to the fact that, in highly emaciated fat-tissue, cells are often found which exhibit a proliferation of their nuclei, and even contain a large number of "young cells." He terms this condition the "proliferating atrophy," in contradistinction to the simple "serous atrophy." Czajewicz asserts that the fat in rabbit disappears after a few days' abstinence from food, but rapidly re-appears in the original globules upon the resumption of abundant feeding. The substance which under these conditions replaces the fat is said to be serum or mucus. In inflammation, the same observer noticed a splitting of the fat-globules into numerous plastids.

From all these facts we may conclude that fat-tissue is closely allied to myxomatous connective tissue, although the metamorphosis in each is materially different. A certain number of plastids changed to fat may coalesce into what we know to be a territory, in which unchanged portions of bioplasson are left.

* Lehrbuch der Gewebelehre. 1877.

Around the territory a connective-tissue capsule originates, in a way similar to the formation of the myxomatous reticulum of fibers, and the nucleus in the capsule of the fat-globule is analogous to the nuclei found at the points of intersection of the myxomatous reticulum.

(2) ***Striated or Fibrous Connective Tissue.*** The term "connective tissue" was employed by Johannes Müller, in 1835, for designating the *tela cellulosa* of older anatomists. B. Reichert, in 1845, first maintained the continuity of this tissue, and, considering it to be structureless, attributed the fibrous appearance to the presence of folds or striations. Virchow, in 1851, demonstrated the presence of corpuscles, the supposed hollow and so-called "connective-tissue cells," imbedded in the fibrous intercellular substance; and W. Kühne, in 1864, proved by the means of electricity that these corpuscles possess vital properties—viz., contractility.

At present we know that the tissue corpuscles, being bioplasson formations, are imbedded in cavities of the basis-substance. The latter is eminently glue-yielding, and composed of numerous delicate spindles, arranged in lines. It is only after teasing of the specimen that an isolated fiber is discovered, while in the continuity of the tissue isolated fibers are not observed.

We know, furthermore, that the fibrous basis-substance (synonymous with the matrix and intercellular substance of former histologists) is traversed by a delicate reticulum of living matter, whose meshes present an almost uniformly rectangular arrangement. This reticulum is visible within delicate bundles in specimens preserved in chromic acid, without the addition of any re-agents; or in other specimens by the use of re-agents, as described before (page 122). The alcohol treatment (page 141) also serves for bringing the reticulum to view.

The basis-substance varies greatly in its degrees of density. It is very dense in the tendon, the sclerotic, the cornea, and less dense in the formations termed "loose connective tissue." The delicate spindles, which constitute the fibrillæ by coalescing in a longitudinal direction, are separated from each other by a less dense so-called cement-substance, while bundles of fibers are separated from each other by a more liquid substance, which, as a rule, contains, besides the blood-vessels and lymphatics, numerous plastids, all being connected with each other as well as with the walls of the vessels and the reticulum in the basis-substance proper. In some varieties of this tissue the basis-substance,

instead of being fibrous, is composed of ribbon-like formations, as in the periosteum; and in others it is disposed of in flat layers, as in the cornea. In many instances we meet with an extremely dense basis-substance, termed the elastic substance, which either occurs in the shape of fibers at the boundary of territories, or almost entirely replaces the glue-yielding basis-substance. This formation appears in the shape of either a dense reticulum or a uniform flat layer. Examples of fibrous elastic basis-substance are found in the connective tissue of the derma of the skin, in the periosteum, etc.; examples of an elastic reticulum are furnished by the Lig. nuchæ, the adventitial coat of arteries, etc.; examples of flat elastic layers are found in all the so-called "hyaline or structureless membranes," beneath epithelial and endothelial formations, in the sarcolemma, etc.

The different varieties of fibrous connective tissue may be classified according to the following characteristics:

Delicate bundles of fibrous tissue, running mainly in one direction, and being separated by a basis-substance of slight density, form the so-called loose connective tissue—f. i., in the omentum and the arachnoid;

Bundles of fibrous connective tissue, interlacing in all directions, produce a felt-work structure—f. i., in the derma, the interarticular ligaments, the sclerotic;

Coarse bundles arranged in only a longitudinal direction are found in the tendons and in the articular ligaments;

Flat bundles transformed into ribbons, freely interlacing, appear in the periosteum, the dura mater, the pericardium, and the aponeuroses;

A coalesced layer of elastic basis-substance produces a flat, sheet-like formation—f. i., in the hyaline or basement layers, and in sarcolemma;

Lamellated layers of considerable breadth, freely interlacing, build up the cornea.

(a) Delicate Connective Tissue Composed of Fibrillæ, or of Comparatively Thin Bundles of Fibrillæ. This variety, usually termed "loose connective tissue," is arranged in bundles, in which the fibers are connected by a small amount of a cement-substance, soluble in lime and baryta water. Between the bundles are spaces which contain either a semi-fluid, viscid, myxomatous basis-substance or a lymph-like liquid. These spaces may become expanded by accumulation of a serous liquid, as in œdema, or of air or liquids introduced from without.

The plastids in the bundles are flat corpuscles, either irregularly scattered or presenting a chain-like arrangement; these bodies are frequently small, not surpassing the size of nuclei. In the myxomatous portion, however, they are larger, and have coarse offshoots, sometimes directly joining in a stellate form. The myxomatous portion may also contain, in a varying number, the "migrating cells" of Von Recklinghausen and the coarsely granular "plasma-cells" of Waldeyer, especially in the neighborhood of capillary blood-vessels. Their significance is not yet understood, nor is their presence constant.

The delicate bundles, if treated with dilute acetic acid, swell and are constricted in such a manner as to give the bundle an hour-glass or rosary-like appearance. These constrictions are due, according to Henle, to the presence of elastic fibers twined around the bundle, which are not acted upon by the acetic acid. Their origin is explicable, as I shall show hereafter, by the formation of territories, a number of which compose the bundle, while at the boundaries of the territories the basis-substance is solidified into elastic substance. A. Rollett maintains that the elastic fibers are offshoots of cells similar to the reticular variety of connective tissue; according to Franz Boll, these cells, originally twined around the bundle in shape of a reticulum, fuse in advancing development into an elastic membrane, which envelops the bundle and exhibits linear thickenings, branching after the manner of veinlets in leaves.

FIG. 55.—ARACHNOID OF THE SPINAL CORD OF AN ADULT.

Delicate bundles of fibrous connective tissue, *B*, run in different directions and contain very small plastids in the shape of oblong nuclei. The interstitial basis-substance slightly fibrous. *E*, a portion of the covering endothelium. Magnified 500 diams.

The best examples of loose connective tissue are the arachnoid and the trabeculæ traversing the sub-arachnoideal space. (See Fig. 55.)

In serous membranes, especially in the omentum, the delicate bundles of fibrous connective tissue are arranged in the shape of a reticulum, the meshes of which are very large, constituting what has been termed "areolar connective tissue" (Hassal).

The fibrillæ, composing delicate bundles, freely interlace in the papillary layer of the derma of the skin, and in the mucous membranes; while in the subcutaneous tissue the bundles are coarser and their interstices contain the fat-lobules. Similar features are observed in the loose connective tissue around the eyeball and in the female breast.

The delicate bundles of the pia mater are also interlaced, and generally enter the gray cortex of the brain and the white cortex

FIG. 56.—DELICATE FIBROUS CONNECTIVE TISSUE FROM THE BORDER OF THE THYROID CARTILAGE OF A YOUNG MAN.

C, cartilage, *B*, *V*, blood-vessels in transverse and oblique section; *G*, dense fibrous connective tissue. Magnified 800 diameters.

of the spinal cord in radiating directions. They are freely supplied with blood-vessels in their interstices, and upon entering the nervous tissue gradually divide, and their fibers form a delicate reticulum which supports the nerve-formations, the "neuroglia" of Virchow.

In muscle, a delicate loose connective tissue is found around the muscle-fibers and their bundles (perimysium internum and

externum); this tissue, especially in its juvenile condition, i freely supplied with large and branching plastids.

Delicate fibrous connective tissue is often largely intermixe with other varieties of connective tissue in the form of eithe scattered fibrillæ or interlacing bundles of fibrillæ. It blen with the true myxomatous tissue, as well as with the den fibrous varieties. Bundles of the latter, in the tendon and th interarticular ligaments, are surrounded and inclosed by loo

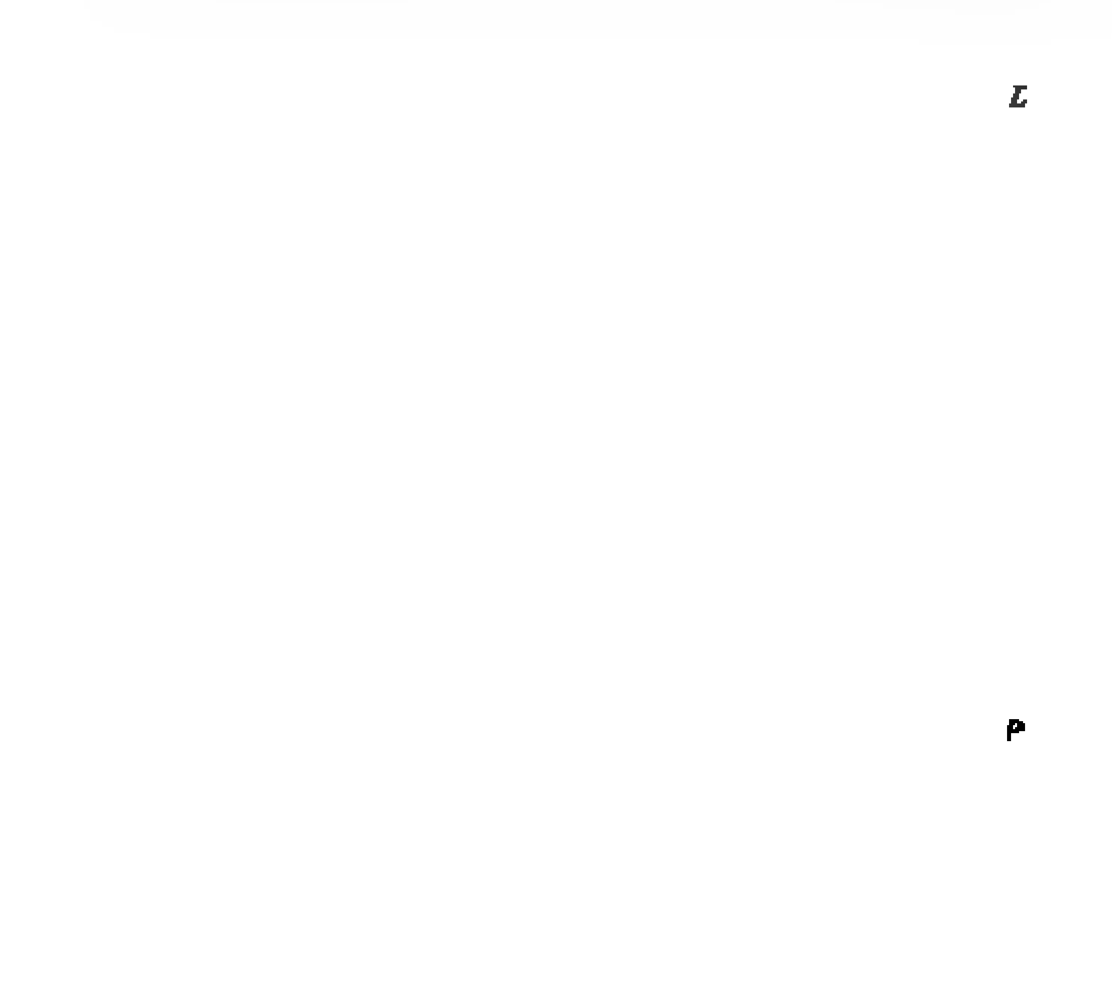


FIG. 57.—INTERARTICULAR LIGAMENT FROM THE KNEE-JOINT OF A GROWN DOG.

L, bundles cut in a longitudinal direction; *C*, bundles cut in a transverse directi the nucleated, finely granular plastids forming a continuous layer around the bundles. nified 500 diameters.

connective tissue, which is the exclusive carrier of blood-ves (See Fig. 56.)

(b) Dense Connective Tissue composed of Coarse Interla Bundles. The essential feature of this variety is the pres of comparatively coarse bundles, which, interlacing ei at right angles or in an oblique direction, produce a

firm and dense felt-work. The bundles exhibit scattered oblong or spindle-shaped plastids, often reduced to the size of nuclei. The interstices between the bundles, the interfascicular spaces, being filled with a more or less liquid substance, contain a continuous layer of plastids and a few blood-vessels. The bioplasson is freely supplied with nuclei, and by its arrangement between and around the bundles presents a reticulum similar to that in the myxomatous tissue of the umbilical cord, the difference being that in the latter the meshes contain a jelly-like, myxomatous basis-substance, in the former a solid, fibrous one. The peripheral portions of the intervertebral disks and the interarticular ligaments are examples of this tissue. We may cut through such a tissue in any direction, and invariably meet with longitudinal, oblique, and transverse sections of bundles. While the longitudinal sections exhibit a dense striation or fibrillation, the transverse sections look homogeneous or slightly dotted, corresponding with the transverse sections of the fibrillæ. (See Fig. 57.)

FIG. 58.—SCLEROTIC OF THE BULL'S EYE. VERTICAL SECTION.

L, bundles cut in a longitudinal direction; *T*, bundles cut in a transverse direction, *O*, bundles cut in an oblique direction; *P*, the continuous interstitial bioplasson layer, containing numerous pigment granules. Magnified 500 diameters.

In the derma of the skin, the bundles or groups of bundles are coarser the nearer they are situated to the subcutaneous tissue; toward the surface they gradually become finer, and in the uppermost portion, the papillary layer, the bundles are extremely delicate. In the derma, too, the bundles are separated from each other by a continuous layer of nucleated

plastids, and in this layer scanty capillary blood- and lymph-vessels are found. Both blood- and lymph-vessels ramify the more the nearer they approach the surface, so that the papillary layer has the greatest number of vessels. In every direction we meet with longitudinal, oblique, and transverse sections of bundles, the latter being characterized by a dull luster and a homogeneous or finely dotted appearance. At the periphery of the bundles we see elastic fibers branching at acute angles, in correspondence with the territories composing a bundle. The elastic basis-substance is

1
2
3
4
5
6
7
8

FIG. 59.—TENDON OF ACHILLES IN A LONGITUDINAL SECTION. STAINED WITH CHLORIDE OF GOLD.

1–8 are the bundles, between which the interfascicular spaces are seen; T, torn bundles exhibiting isolated fibrillæ. Magnified 100 diameters.

marked by yellow color and high degree of luster; it increases in amount with the age of the individual.

The *sclerotic* shows bundles and groups of bundles, interlacing usually at right angles. In transversely cut groups we see that the single bundles are separated from their neighbors by a cement-substance, which, on account of its lower degree of density, refracts the light less than the basis-substance of the bundles themselves. The groups of bundles are separated by a continuous layer of bioplasson, which therefore exhibits a reticular arrangement. In specimens from the sclerotic of dark-colored cattle this bioplasson layer is very prominent, owing to the presence of black pigment granules. (See Fig. 58.)

(c) Dense Connective Tissue composed of Coarse Bundles running in a Longitudinal Direction. The principal representative of this variety is the tendon.

In thin sections from a fresh tendon, or a tendon preserved in chromic acid solution, either stained with chloride of gold or not, we recognize with lower powers of the microscope that the tendon is made up of bundles of a finely striated tissue. All bundles are spindle-shaped, and vary greatly in size; they are separated from each other by light interstices, in which, particularly in the injected specimens, the blood-vessels are seen to course along and around the bundles. The appearance of a bundle is striated as long as the continuity of the tissue is unbroken. But where the

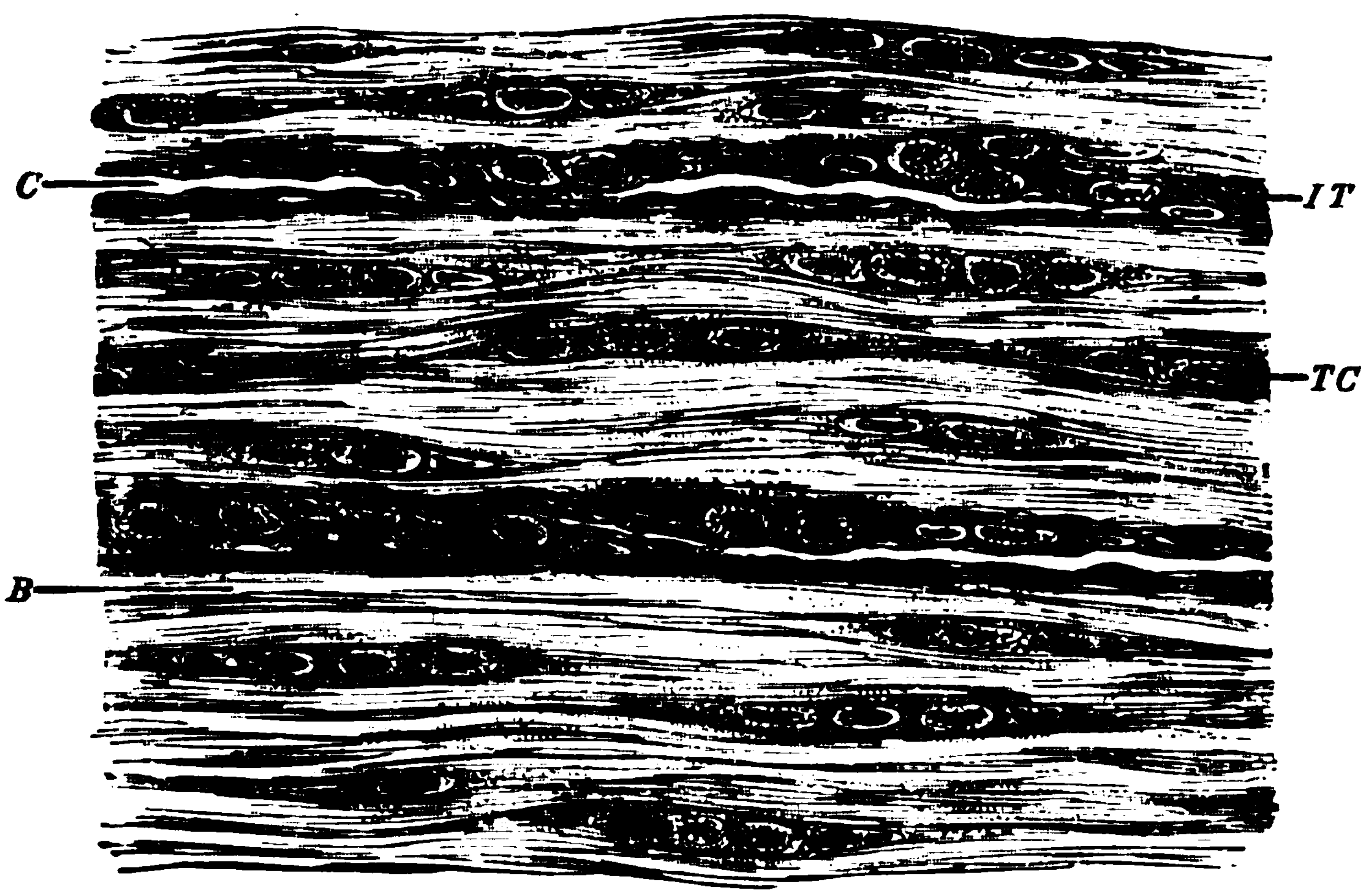


FIG. 60.—TENDON OF ACHILLES OF A YOUNG PERSON. LONGITUDINAL SECTION. CHROMIC ACID SPECIMEN.

B, bundles of striated connective tissue, here and there finely dotted; *TC*, tendon corpuscles within the bundles or between the smallest bundles; *IT*, interstitial medullary tissue carrying capillary blood-vessels, *C*. Magnified 500 diameters.

razor has torn the bundle, isolated fibrillæ appear, which, owing to their elasticity, retract and curl. (See Fig. 59.)

Higher amplifications reveal that the larger bundles divide into a number of smaller ones, all of which exhibit a spindle shape, and in correspondence with the boundary lines of the secondary bundles we see spindle-shaped plastids, either single or in rows or chains, and either nucleated, and, as a rule, pale granular, or reduced to the size of homogeneous or granular nuclei. All of these are included under the term "tendon corpuscles." In advanced age the apparently isolated nuclei prevail, especially in the middle of the tendon, while in younger

individuals, and at the periphery of the bundles at any age, the rows and chains are more numerous. The interstices between the larger bundles contain, besides a few capillary blood-vessels, a large number of nucleated plastids, either isolated or united in a continuous layer. The sum total of these plastids, together with a slight amount of basis-substance, constitutes what we have called (see page 147) medullary tissue. In advanced age the medullary corpuscles are much less numerous, and a loose fibrous connective tissue carries the blood-vessels. Elastic fibers are, as a rule, not present at the borders of the bundles. A comparison between the plastids within and those between the bundles shows them to be alike in size and general appearance, with the only difference that those within the bundles are relatively few in number, while those in the interstices are very numerous. The view can, therefore, be maintained that between the larger bundles there are numerous, and between the small fasciculi, composing one bundle, there are few, plastids—a view which, as I shall later on demonstrate, proves useful for understanding the structure of the tendon as well as its development. (See Fig. 60.)

In the transverse section of a tendon we notice fields of basis-substance very finely dotted, the dots being the transverse sections of the fibrillæ. In the bundles we recognize the granular, usually nucleated, plastids or tendon corpuscles, with numerous stellate offshoots, the "wings" of authors. Offshoots connect the plastids with each other and with the medullary tissue, or the loose fibrous connective tissue, present in the interfascicular spaces. The smaller bundles do not usually show distinctly marked outlines, as neighboring bundles frequently coalesce, and are not separated by offshoots of the tendon corpuscles. When we recall the spindle shape of each bundle, we can readily understand why their sizes vary in transverse section. We may call a bundle a field which is completely surrounded by interfascicular tissue, and contains in its *center* a branching plastid, or, we may say, a larger bundle is composed of a number of smaller ones, though not distinctly separated, *between* which lie the branching plastids. The blood-vessels are met with only in the interfascicular spaces, running both in transverse and longitudinal directions; they penetrate the tendon through the tenaculum, which connects it with its sheath, and the elongations of which constitute the interstitial formations between the tendon bundles. (See Fig. 61.)

In old animals, the loose interfascicular connective tissue is sometimes found freely supplied with elastic fibers. As Treitz and Kölliker have shown, the tendons attached to smooth muscle bundles are composed mainly of elastic fibers. L. Ranvier discovered at the periphery of the bundles of tendon flat "cell-plates," arranged in rows, exhibiting elastic ridges, either single or in numbers up to five. His method of examination of tendon is teasing and pulling, and he pulled from preference rats' tails, in order to obtain the broken, fringy ends of the delicate tendons along the vertebral column. After he had pulled and severed the tendons, he transferred the fringe to the glass slide, and, in order to prevent it from shrinking, sealed it at both ends to the slide. Although this method is not very inviting, pulling rat-tails became quite fashionable in the laboratories in Europe a number of years ago. Ranvier denies the existence of cell-formations in the tendon other than the endothelial plates. Perhaps these are flat, endothelial investments of the larger bundles

FIG. 61.—TENDON OF ACHILLES OF A YOUNG PERSON. TRANSVERSE SECTION. CHROMIC ACID SPECIMEN.

B, bundles finely dotted; *C*, tendon-corpuscle with offshoots, connecting with the interfascicular tissue, *IT*; the latter contains the capillary blood-vessels, *BV*. Magnified 500 diameters.

similar to the investing sheath of Boll, unquestionably present around the periphery of the tendon. Löwe has maintained that such an investment is also found around the bundles of the tendon, but he has been contradicted by other observers. The elastic ridges are probably the place of attachment of neighboring bundles.

One of the greatest difficulties encountered by former observers was to explain satisfactorily the wing-like offshoots of the

tendon corpuscles seen in transverse sections, as no trace of such formations is visible in longitudinal sections. This difficulty was overcome by the discovery of offshoots of the tendon corpuscles, brought into view in longitudinal sections by the silver and gold staining. The minutest features in the structure of the tendon are described on page 122, and illustrated in Fig. 37 and Fig. 38.

The *articular ligaments* are formations closely allied to tendon; between their bundles, however, a greater amount of loose connective tissue is found than in the tendon.

(d) Dense Connective Tissue composed of Interlacing Ribbons. This variety is essentially constructed in the same manner as tendons, but instead of spindle-shaped bundles, we find flat, rhomboidal ribbons. Periosteum is representative of this tissue, a description of which is given on page 125. The elastic fibers border each ribbon or subdivide it into smaller rhomboidal fields, a feature which is explicable by the history of development of the territories of the ribbons.

In the dura mater and the pericardium, the bundles are distinctly striated and not quite so flat as those in the periosteum.

In aponeuroses, the bundles, in accordance with the general sheet-like form of this tissue, are flattened and interlaced, chiefly in a rectangular direction. The interstices between the bundles are quite narrow, but plastids are observed here as well as in the tendon. C. Ludwig, who forced colored liquids into these interfascicular spaces, mistook the beautiful rectangular reticulum thus obtained for lymph-spaces. Formations kindred to aponeuroses are the fasciæ and the tendinous capsules of different glandular organs—f. i., the capsule of the kidney, the albuginea of the testis, the sheath of the cavernous bodies of the penis, etc.

In some ligamentous formations, such as the Lig. sub-flava of the vertebræ, the Lig. nuchæ, the membr. thyro-cricoidea, the Lig. stylo-hyoideum, etc., the fibrous basis-substance is almost completely transformed and condensed into the yellow, elastic substance which appears in the form of branching reticular fibrillæ, between which are scantily found bundles of striated connective tissue.

(e) Coalesced Layers of Elastic Basis-substance, arranged in a sheet-like manner, are often found at the borders of connective-tissue formations, close beneath epithelial and endothelial layers. They bear the names of hyaline, structureless, or basement membranes, in contradistinction to "cuticular formations" of a similar

appearance found between epithelial layers—f. i., between the root-sheaths of the hair.

Elastic membranes certainly are not structureless, but exhibit a reticulum of living matter of extreme delicacy, concealed in the fresh condition by the highly refracting elastic basis-substance. I am positive that such a reticulum is present in Bowman's and Descemet's layers of the cornea. By means of this reticulum, the connective tissue is held in living union with the epithelium. Such membraneous formations may vary greatly in width, even in the same tissue,—f. i., the cornea,—and sometimes they may be entirely absent. They, when present, resist the action of acids and alkalies, and, to some extent, the inflammatory process.

Elastic membranes of the connective-tissue series are the following: Bowman's layer at the outer and Descemet's layer at the inner surface of the cornea; the capsule of the crystalline lens and the hyaloid membrane of the vitreous body; the layer between the outer root-sheath and the follicle of the hair; the elastic layer beneath the endothelial coat of larger arteries; and the investing, sometimes fenestrated, layers beneath epithelia of glands—f. i., the salivary, the mammary glands. In the kidneys, the connective tissue of the capsule of the tuft, also that which lies between the tubular formations, contains a large amount of elastic substance, which produces a very firm support for the epithelia.

The striated muscle-fibers, with the exception of those of the heart, are invested by an elastic membrane, termed sarcolemma; so are the medullated nerves around the axis-cylinder and around the myeline—*i. e.*, axis-cylinder sheath and myeline sheath.

(f) Lamellated Layers of Fibrous Interlacing Connective Tissue. The only representative of this variety is the cornea of the eyeball, the basis-substance of which, although morphologically closely allied to that of elastic substance, is chemically different from both "elastine" and "chondrine." A. Rollett (1859) proved that the "amorphous" basis-substance of former histologists consists of bundles of connective tissue, which are connected by a kind of cement-substance soluble in lime-water and in baryta-water. The main feature of the cornea is that the bundles join to form very thin flat layers, the lamellæ; while these lamellæ themselves are connected by somewhat looser bundles, traversing the less condensed interstices between them.

In the fresh cornea no trace of plastids (cornea corpuscles) is visible; but if the cornea be kept in an indifferent liquid, after a

while faint traces of these corpuscles become perceptible, exhibiting a few scanty offshoots. The shape of these corpuscles varies greatly in different portions of the cornea, as well as in the cornea of different animals.

A clear idea of the nature of the cornea corpuscles can be obtained only by resorting to re-agents. Von Recklinghausen (1862) first brought to view the beautiful light and branching spaces in a dark basis-substance by applying nitrate of silver. He considered them as lymph-spaces or juice-canals, supposing them to be the beginnings of the lymphatics proper. In these spaces, he thought, the "cornea-cells" were suspended. (See Fig. 62.)

FIG. 62.—LAMELLA OF THE CORNEA OF A GROWN CAT, STAINED WITH NITRATE OF SILVER.

S, light branching spaces with serrated edges, traversing the dark brown granular basis-substance. *B*, *F*, fibers connecting the lamellæ and torn by the process of splitting the lamellæ. Magnified 600 diameters.

Later researches have shown that the "lymph-spaces" of the cornea are closely related to the cornea-cells, which were meanwhile demonstrated by W. Kuehne (1864) and others to be composed of contractile protoplasm, and endowed with properties of life. The method of gold-staining has proved to be the most valuable for revealing the structure of the cornea corpuscles and their relation to the basis-substance. (See Fig. 63.)

Researches on the Microscopical Structure of the Cornea. By William Hassloch, of New York.*

It is generally acknowledged that the substantia propria of the cornea is made up of fibrils united into fascicles; that the majority of these bundles, by being more or less parallel to the surface of the cornea, form the laminated structure of the latter, at the same time crossing one another, and so giving rise to a kind of lattice-work; while other fibers and bundles traverse the cornea in various directions. The fibrils, as well as the fascicles and lamellæ, are connected with one another by an intermediate cement-substance, which somewhat differs from the fibrils in its chemical reaction.

Fig. 63.—Lamella of the Cornea of a Grown Cat, Stained with Chloride of Gold, after Previous Treatment with Dilute Lactic Acid.

C, dark violet nucleated cornea corpuscles, traversing the pale violet granular basis-substance, *B*. *N*, nerve-fibrillæ, connecting with cornea corpuscles. Magnified 500 diameters.

But, concerning the relation of the protoplasm to the basis-substance, observers are of very different opinions. Some of them do not admit the existence of the protoplasmic bodies at all, asserting that within the basis-substance of the cornea only a tubular system is present, lined with "cell-plates." Other histologists hold the view that there is a certain quantity of protoplasm (cells of the cornea) inclosed in the "serous spaces," in which it ramifies, but which it does not completely fill. One of the most prominent advocates of the latter opinion is W. Waldeyer,† deriving his views chiefly

* "Archives of Ophthalmology and Otology," vol. vii., 1878.
† Article "Cornea," in Graefe-Saemisch's Hand-book, 1874.

from the results of injections made by him and other recent observers into the tissue of the cornea. Fluids, pressed into the corneal parenchyma, produce, indeed, ramified figures resembling the "corneal corpuscles." W. Kuehne, S. Stricker, and A. Rollett state that there are complete corneal cells with protoplasmic bodies, with nuclei and nucleoli, within the ramifying spaces, and that they fill these spaces completely. W. Engelmann denies the existence of preformed spaces inclosing corneal cells, etc. He states that there are spaces containing nothing but protoplasm, and this is, in my opinion, the only correct view, as I shall endeavor to prove.

In order to study the relation of the protoplasm to the basis-substance, I chose the cornea of the dog and of the cat, giving preference, after repeated trials, to that of the cat, as has previously been done by S. Stricker, on account of its easy splitting. With some practice one may succeed in obtaining lamellæ which present two or even only one layer of corneal corpuscles, and which, therefore, are sufficiently transparent to admit of being examined even with the highest powers of the microscope.

FIG. 64.—LAMELLA OF CORNEA OF A CAT, AGED ONE YEAR AND A HALF, STAINED WITH A TWO PER CENT. SOLUTION OF NITRATE OF SILVER. TWO LAYERS. [PUBLISHED IN 1878.]

S, light fields with pale granular contents, faintly marked nuclei, and coarse and fine processes. Every light field has perforated borders, and thus abundantly communicates with a delicate light net-work which traverses the dark brown basis-substance, *B*, in all directions. Magnified 1000 diameters.

To stain the cornea, I at first tried nitrate of silver. The cornea of a cat was taken out immediately after death, and was put into a two per cent. solution of nitrate of silver for one-half to one hour; then it was washed with distilled water, and, finally, for several days left under the influence of a very mild dilution of acetic acid. Instead of the acetic acid, in later experiments, I substituted lactic acid, which proved even more satisfactory than the former. After being prepared in this way, the cornea of the cat was ready

to be split into lamellæ. The specimens were mounted with equal parts of glycerine and water.

With enlargements of 300–500 such lamellæ show in a dark ground—basis-substance—light fields with numerous connecting branches, generally known as Von Recklinghausen's serous canaliculi; and even an enlargement of 500 is sufficient to prove that the outlines of these light spaces do not appear smooth at all, but granular—viz., abundantly perforated, and that the brown or gray-brown looking basis-substance is finely granular.

With higher powers (immersion lenses, with enlargements of 800–1200) the following facts are observed: Within the light spaces oblong nuclei, with very faint contours and a great number of extremely pale granules, are visible. The light spaces are connected with their neighbors by light processes of various sizes, traversing the basis-substance. The borders of these light fields and their branches are abundantly perforated, like a sieve, throughout, so that true outlines do not exist. Fine, light tracts run from every light space and its branches through the basis-substance, profusely ramifying and anastomosing, sometimes radiating, and thus forming an extremely delicate light net-work, the threads of which traverse the basis-substance in all directions, and connect with the light fields and their processes at the whole circumference. What with lower power was recognized as granular structure is by higher enlargements elucidated as a very fine light net-work, the meshes of which are filled by the dark brown basis-substance. (See Fig. 64.)

FIG. 65.—CORNEA OF A CAT, TWO YEARS OLD, STAINED WITH NITRATE OF SILVER. TRANSVERSE SECTION. [PUBLISHED IN 1878.]

S, light fields containing fine pale granules, with coarse and fine light offshoots. *N*, nerve-fibers in connection with the light reticulum, which traverses the dark brown basis-substance, *B*, throughout. Magnified 1000 diameters.

On thin transverse sections the silver-stained cornea of the cat shows the same ramifying light fields as in split preparations, with the only difference that their vertical diameters are notably smaller, while their horizontal diameters are the same as those of the light fields of the lamellæ. The light spaces branch out in all directions, so that not only the light fields of the same stratum are connected with each other, but even those of different layers anastomose by ascending and descending—more or less oblique—processes. Besides these ramifications, especially in the outer strata of the cornea, some fine straight light lines are met with, which, for reasons given below, are proved to be nerve-fibers. On transverse sections, also, the brown basis-substance is traversed by light ramifying tracts, to such an extent that the

cement-substance cannot be distinguished from the other components of the cornea. (See Fig. 65.)

Further, I tried to stain the cornea of the dog and of the cat with chloride of gold. Many experiments failed, though I had exposed the cornea to the influence of the chloride of gold for hours. The after-treatment with acetic and tartaric acid gave only negative results. I could never see distinct cornea corpuscles with their ramifications until, at last, by the aid of lactic acid, I succeeded in obtaining specimens of such beauty and clearness, that all doubt with regard to the finest structure of the cornea disappeared.

My method is the following: The cornea of a cat is taken out immediately after death, soaked in a ten per cent. solution of lactic acid for a period of about twelve hours; then during one or two hours it is kept in a one-half per cent. solution of chloride of gold, slightly acidulated by the addition of a few drops of lactic acid, and finally exposed to the influence of daylight. The superficial strata of the cornea and a peripheral border of one mm. turn yellow,

B

P

FIG. 66.—LAMELLA OF THE CORNEA OF A CAT, TWO YEARS OLD, SOAKED IN DILUTED LACTIC ACID AND THEN STAINED WITH A ONE-HALF PER CENT. SOLUTION OF CHLORIDE OF GOLD. [PUBLISHED IN 1878.]

P, dark violet fields, the cornea corpuscles, the nuclei of which are mostly hidden, with offshoots of different sizes. The cornea corpuscles and their offshoots are connected with a dark violet net-work traversing the pale violet basis-substance *B*; the latter net-work shows broader meshes than that of the corpuscles and their branches. Magnified 1000 diameters.

and are of no use for examination, but the other part, the characteristic purplish tint of which shines through the yellow envelope, is invaluable for research. After having made the above described experiments, I learned that F. S. W. Arnold, of New York, had previously used lactic acid for the reduction of chloride of gold; but he informed me that his method differs from mine, inasmuch as he uses the chloride of gold in the first stage of the preparation, followed by the lactic acid—just the reverse of my plan of treatment.

The cornea of the cat, prepared after my method, splits readily, and its lamellæ, after turning dark enough by the influence of daylight, appear under the microscope throughout their whole extent strewn over with numerous, richly ramifying, dark violet corpuscles. In many of the latter the nuclei are distinctly visible; the corpuscles themselves crowded with dark granules; the basis-substance light, pale violet, and also having a granular appearance. I have searched through a great many lamellæ, but I have never found any corpuscles that did not shoot off into branches; everywhere and always I met with only ramifying, dark violet corpuscles, with numerous connections and in different strata of varying sizes. The dark violet fields fully coincide with the light spaces of the silver-stained cornea as to size, figure, and connections, as has been stated by W. Kuehne. The only difference is that in the silver

FIG. 67.—LAMELLA OF THE CORNEA OF A CAT, TWO YEARS OLD, STAINED WITH A ONE-HALF PER CENT. SOLUTION OF CHLORIDE OF GOLD, AFTER HAVING BEEN SOAKED WITH DILUTED LACTIC ACID. [PUBLISHED IN 1878.]

P, dark violet fields, the cornea corpuscles, with only a few broad offshoots, but numerous dark violet, thread-like connections, non-medullated nerve-fibers, *N*, the latter partly traversing the cornea corpuscles and partly joining the net-work of the same; between the cornea corpuscles and the net-work of the basis-substance, *B*, extremely fine retiform connections are present, the latter net-work also connects with delicate nerve fibrillæ, *E*. Magnified 1000 diameters.

specimen light fields are visible in a dark ground, while in the gold specimen the dark corpuscles appear in a light ground—pictures which correspond with each other as the negative with the positive photograph.

Gold specimens examined with high powers (800–1200) show that the dark violet ramifying corpuscles, without exception, have a retiform structure, and that the nucleoli, the contours of the nuclei, and all the granules are connected with one another by innumerable fine threads. The whole net-work

is tinted equally dark violet, while its extremely narrow meshes appear pale violet. (See Fig. 66.)

The borders of the corpuscles and their branches are nowhere distinct; contours in the real sense of the word are wanting in the gold specimen as well as in the silver specimen, inasmuch as from the whole circumference of these ramifying, dark violet fields immense numbers of fine threads protrude, to join their neighboring dark violet granules within the basis-substance. The examination of any portion of such a specimen will not fail to convince the observer that also in the basis-substance nearly all dark granules are interconnected by fine threads. The cause of the difference between the shade of the cornea corpuscles and that of the basis-substance is, that in the former the granules are larger and lie close together, and consequently the meshes are very small, while within the basis-substance the granules are mostly fine and more dispersed, and for this reason are separated from one another by larger meshes.

In some lamellæ, and, as it seemed to me, principally in the outer layers of the cornea, many corpuscles are connected with one another, not by broad branches, but by dark violet, more or less straight lines, which, for their characteristic rosary-like structure must be considered non-medullated nerve-fibers. (See Fig. 67.)

In profile, the gold-stained cornea of the cat offers another proof of the coincidence of the positive gold image with the negative silver specimen.

FIG. 68.—CORNEA OF A CAT, TWO YEARS OLD, STAINED WITH A ONE-HALF PER CENT. SOLUTION OF CHLORIDE OF GOLD, AFTER BEING TREATED WITH DILUTED LACTIC ACID. TRANSVERSE SECTION. [PUBLISHED IN 1878.]

P, dark violet fields with broad branches and with fine offshoots, the latter being nerves. *N*; the net-work of the dark fields everywhere is in connection with that of the basis-substance, *B*. Magnified 1000 diameters.

Flat, elongated, dark violet bodies are visible, which, in the horizontal direction, anastomose with one another by means of fine long processes; while broad, rather oblique, dark violet branches ascend and descend to connect the corpuscles of different layers. The net-work of the dark fields and that of the basis-substance are shown with the same clearness as in split specimens. The laminate structure of the cornea is just as imperceptible in these transverse sections as it is in those of the silver-stained cornea. (See Fig. 68.)

In transverse sections of the gold-stained cornea of a dog I observed, especially in the central parts of the cornea, formations which sufficiently explain

he views of W. Waldeyer, who maintains that the cornea corpuscles do not ompletely fill the "serous spaces." There I saw groups of cornea corpuscles rhich leaned mainly against one of the walls of the space, while a more r less considerable portion of the latter appeared empty. A closer examnation, however, proved that these apparent voids are artificial products, amely, vacuoles. It can be observed that the eccentric cavity is situated *vithin* the cornea corpuscle, and on its whole circumference is inclosed by the rotoplasm of the cornea corpuscle. No matter how thin the strip of prooplasm which is interposed between the vacuole and the periphery of the 'serous space" may be, it is always present. It is known that such vacuoles an arise from contraction of the living matter within the protoplasm. The uestion why these contractions, perhaps as a result of the action of the hloride of gold, were observed only in certain groups of cornea corpuscles, emains unsolved. In the cornea of the cat I have never met with any formaions of this kind.

From these observations it clearly follows *that a tubular system, as escribed by Von Recklinghausen, does not exist in the cornea at all.* The light elds which the silver specimens of the cornea show are not "serous paces," but protoplasmic bodies, as stated by W. Engelmann and others, viz., paces which are wholly filled with protoplasm. The strongest proof of this ssertion is found in the result of the method of staining the cornea with loride of gold, improved by the treatment with lactic acid, as it exhibits the rnea corpuscles in perfectly clear images, which in every particular correond to the negative silver images. Whether an interstice filled with fluid mains between the wall of the so-called serous space and the protoplasmic dy or not, I will not yet venture to decide; but as the protoplasm itself ntains a considerable amount of fluid, it is not necessary to admit the presce of peripheral cavities filled with serum. Wherever an interspace between cornea corpuscle and the wall of the "serous space" can be observed, its esence depends upon the formation of a vacuole, and cannot, therefore, be aintained in opposition to my view. Nor do the parenchymatous injections ove anything contrary to it, for it is apparent that colored fluids, which e forced into the protoplasmic spaces, will press the soft protoplasmic dies against the walls of such spaces, and thus assume the principal forms the latter.

My observations further show that the protoplasm of the cornea corscles has a retiform structure, which can be demonstrated by the abovescribed method of staining the cornea with chloride of gold. The question hether or not this reticulum be an artefact should no longer be a matter of spute, since in the creeping amœba, in colorless blood-corpuscles, and in as-corpuscles the same net-work has been demonstrated, and by photograhy made visible even to the naked eye. That this net-work (nucleoli, borering layer of the nucleus, granules, and connecting threads) is the living atter, the meshes of which inclose the lifeless protoplasmic fluid, is proved s well by the reaction of the chloride of gold, as also by the appearances bserved in inflammation, which S. Stricker has so carefully studied and llustrated.

Finally, my observations show that the living matter thoroughly traverses he fibrous basis-substance of the cornea in the form of an exquisitely delicate net-work, the existence of which is proved beyond all doubt by the correspondence of the negative silver with the positive gold specimens,

though in the fresh condition of the cornea it is as imperceptible as are the cornea corpuscles themselves. If wandering bodies exist within the normal cornea,—I have never met with them,—such bodies will find their paths only in the cement-substance, never within the lamellæ. As the lamellæ are connected with each other by innumerable fine threads of living matter, which

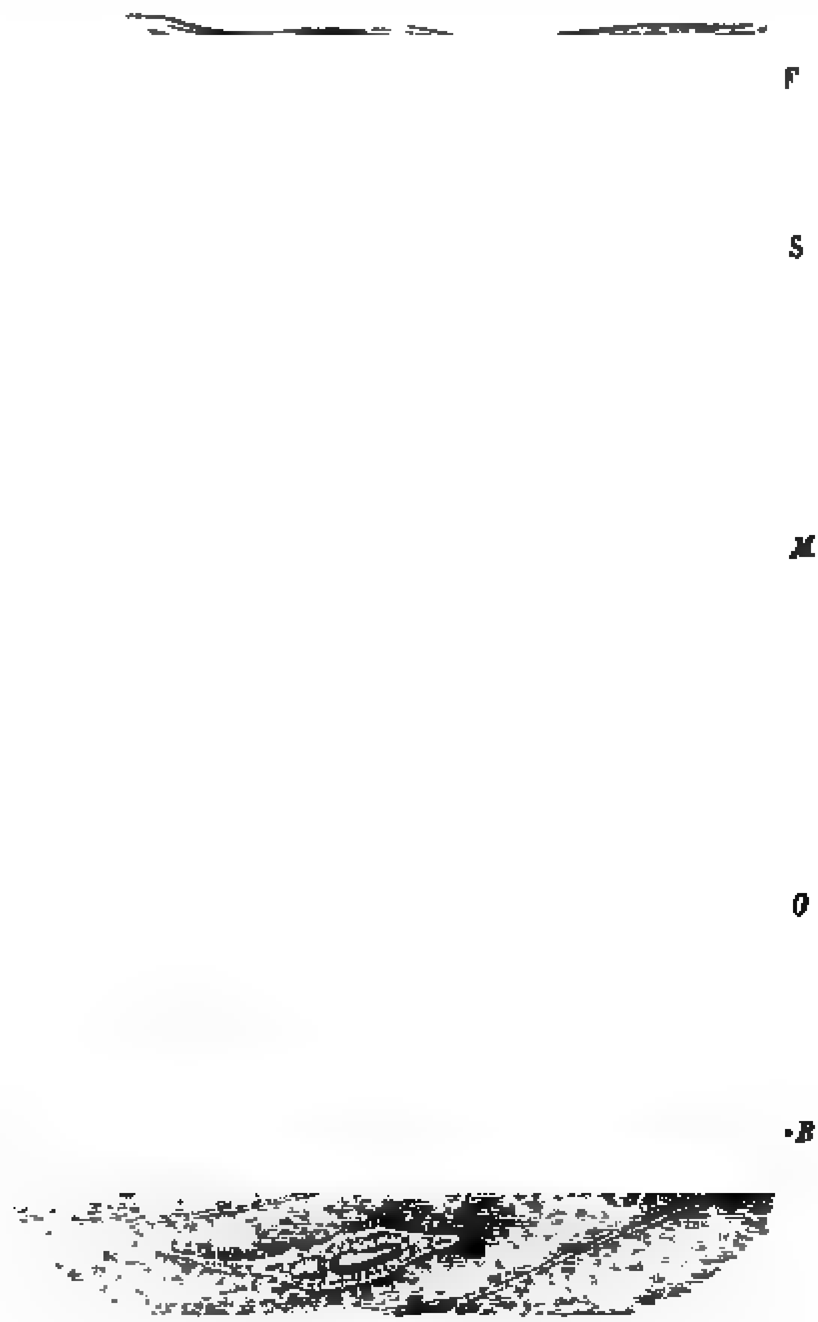


FIG. 69.—PERIOSTEUM OF THE FEMUR OF A NEW-BORN PUP. TRANSVE SECTION. [PUBLISHED IN 1873.]

F, striated tissue of periosteum; *S*, spindle-shaped plastids in the formation of a stri basis-substance; *M*, medullary tissue between the periosteum and the bone; *O*, meda corpuscles in the formation of bone-tissue; *B*, fully developed bone-tissue. Chromic specimen. Magnified 800 diameters.

penetrate the cement-substance,—not taking into consideration the con ing broad, oblique bundles of fibers,—the reason why such wandering b move in zigzag lines is readily comprehended.

As for the finer structure of the cornea, I fully agree with C. Heitzm views regarding the connective tissue in general. The living connecti

the protoplasmic bodies, which this observer has discovered in the myxomatous and fibrous connective tissue, as well as in that of the cartilage and bone, has been successfully demonstrated by me in the cornea also. The living matter presents in connective tissue two different net-works: a narrow one, the meshes of which are filled with fluid,—protoplasm,—and another with broader meshes, traversing the basis-substance.

Development of Fibrous Connective Tissue. This article is a translation of a publication which I made in 1873.* I have nothing to add to the conclusions drawn at that time, but shall make the explanation of the observations a little more detailed.

FIG. 70.—PERIOSTEUM OF THE FEMUR OF A NEW-BORN PUP. LONGITUDINAL SECTION. CHROMIC ACID SPECIMEN, SLIGHTLY STAINED WITH CHLORIDE OF GOLD. [PUBLISHED IN 1873.]

M, layer of medullary corpuscles; *I*, layer of corpuscles in the stage of indifference, preceding the formation of basis-substance, *C* and C_1, spindles of basis-substance of fibrous connective tissue, *E*, elastic ledge. Magnified 800 diameters.

In transverse sections of a shaft-bone of a newly born pup, we recognize between the striated periosteum and the bone-tissue a broad layer of medullary tissue, into which project a few striated bundles of the periosteum proper.† (See Fig. 69.)

* "Untersuchungen über das Protoplasma. IV. Die Entwickelung der Beinhaut, des Knochens und des Knorpels." Sitzungsber. der Kais. Akad. der Wissenschaften in Wien. July, 1873.

† Th. Billroth ("Archiv f. Klin. Chirurgie," Bd. vi.) termed this layer "cambium." A. Rollett ("Manual of Histology," by S. Stricker) illustrates it in a transverse section of the fore-arm bone of a human embryo, five months old.

In longitudinal sections from the surface of a shaft-bone of the same animal, we see in the periosteal tissue different formations corresponding to the stages of development of protoplasma. Between longitudinal bundles of narrow, bright ribbons we recognize fields of corpuscles like those of the medullary tissue, or chains of such corpuscles with distinct vesicular nuclei. Furthermore, we see fields of flat, spindle-shaped protoplasmic bodies of greatly varying size, and with either indistinct nuclei or none. There are fields composed of flat, rhomboidal protoplasmic bodies, some of which exhibit formations like nucleoli. We also meet with fields, the rhomboidal bodies of which appear homogeneous, and slightly shining. Lastly, we encounter ribbons and ledges, composed of very much elongated rhombs, characterized by a peculiar yellowish color and a considerable luster. The slightly shining fields are the *connective-tissue ribbons* proper of the periosteum; while the highly refracting ribbons and ledges are termed *elastic.* (See Fig. 70.)

The examination of good chromic acid specimens, better still such specimens slightly stained with chloride of gold, convinces us that each larger field is separated from the neighboring fields, and within the fields each granular or homogeneous corpuscle from the neighboring corpuscles, by a narrow light rim, which is invariably traversed by delicate grayish spokes. Even in the narrow elastic ribbons a faint transverse striation is here and there seen.

In such a specimen, deeply gold-stained, the differentiation of fields and ribbons disappears, and there become visible at certain intervals spindle-shaped, dark violet bodies, corresponding to the protoplasmic bodies, while the rest of the tissue is split up into a reticulum, with either fine or coarse granules as nodular points.

The periosteal tissue is composed of narrow, spindle-shaped fields, wherever it exhibits a striated or fibrous appearance. In portions made up of broad ribbons, on the contrary, each field represents an elongated rhomb, in which lie, at pretty regular intervals, oblong, flat, nucleated protoplasmic bodies (the "periosteum cells"). Between the rhombs are narrow, bright ledges, the elastic fibers, which either connect several rhombs into large bundles, or subdivide a single rhomb into smaller rhomboidal fields of varying size. At the corners of the rhombs the elastic fibers are interconnected with acute angles.

If, owing to a laceration of the tissue with the razor, a broader, slightly shining ribbon projects from the border of the specimen, we often see at its edge, either on one side or on

both, a very bright strip demarcating the ribbon from adjacent protoplasmic bodies.

In the periosteal tissue of a new-born pup, therefore, we are enabled to trace the transitions of different forms of medullary elements into sometimes narrow, sometimes broad and flat, spindle-shaped protoplasmic bodies. We become convinced that by a gradual change of the latter arise both the "connective tissue" and the "elastic fibers."

The development of the connective tissue in general is a much disputed, and to this day unsolved, question.

In looking over the vast literature on this subject, we may sum up all the views of prominent observers into two theories. One of these may be termed the *secretion theory;* it implies that the intercellular- or basis-substance is produced by a sort of secretion of the cells from an originally homogeneous mass between the cells. The other, which may be styled the *transformation theory,* maintains that the cells themselves are transformed into basis-substance, either by a process of splitting in their entirety, or by a process of transformation of the cell-protoplasm at its peripheral portions.

Secretion Theory. Henle * was the first to assert that an originally homogeneous substance splits into fibrillæ and bundles of fibrillæ. According to Reichert, the homogeneous substance proceeds from a fusion of the cell-membranes with an intercellular substance, and the fibrillæ are only the optical expression of the foldings of this substance. The fusiform cells present in embryonal connective tissue, according to Virchow, Donders, Gerlach, and Kölliker, do not share in the formation of fibers, but persist, as Virchow expressed it, as cells, or are converted into a plasmatic canal-system. The last-named observer is the originator of the idea that the intercellular-substance is a product of secretion of the cells, and this view prevailed for quite a time. Among the recent observers, A. Rollett, L. Ranvier, and I. Kollmann advocate the modified theory that fibrous basis-substance may, to a certain extent at least, originate independently of cells.

Transformation Theory. Th. Schwann † first maintained that the cells, after being elongated, split into bundles. After Max Schultze's discoveries concerning the protoplasma, ‡ the theory of Schwann was modified. Max Schultze held that the fibrous basis-substance of connective tissue arises from a coalescence of embryonal cells composed of protoplasm, and destitute of an investing membrane, and that a thin layer of unchanged protoplasm remains around the nucleus of the primary cell representing the connective-tissue cell. Lionel Beale, in England, § independently of the German observers, expressed similar views; he claimed that the connective tissue is originally made up of elementary parts, consisting of germinal matter, and that subsequently a part of the germinal matter is converted into formed material. According to these views, the originally living protoplasm is, by chemical and morphological changes, transformed into the lifeless basis-substance, though the cen-

* "Allgemeine Anatomie." Canstatt's Jahresbericht, 1845.
† "Mikroskopische Untersuchungen," etc. Berlin, 1839.
‡ Reichert and Du Bois Reymond's Archiv. 1861.
§ "The Structure of the Simple Tissues of the Human Body." 1860.

tral portion of the cell may remain unchanged protoplasm. This theory was adopted, with more or less modification, by E. Brücke, Franz Boll, Waldeyer, and others. Brücke's pupils corroborated the original view of Schwann — viz.: that the fibers of connective tissue originate directly from offshoots of the cells.

Elastic Substance. The elastic fibers, first discovered by Donders,* were thought to be by this observer the product of embryonal fusiform cells which have passed through transitional forms into a plexus of elastic fibers. This view was confirmed, with certain changes adapted to the protoplasma theory, by F. Boll and A. Spina.

Territories. An important discovery concerning the structure of the basis-substance was made by Fürstenberg†—viz.: that certain chemical re-agents may break up the basis-substance of cartilage into globular or polygonal fields, inclosing the central cell. He took these fields, the "territories," for products of secretion of the cells. Virchow‡ corroborated this discovery, and based very important biological views upon their presence (see page 136). He considered the central cell the queen of the territory, and all changes of the latter as depending upon the changes of the cell. R. Heidenhain § also made noteworthy researches as to the territories of the hyaline cartilage.

I have stated on a previous occasion (see page 132) that the *territories*, which are traceable in all higher developed varieties of connective tissue, are the true units of this tissue; so that anybody who understands the development of a single territory understands that of connective tissue *in toto*.

From what I have described as to the basis-substance of the earliest formation,—viz.: the myxomatous basis-substance of medullary tissue (see page 118, Fig. 33 and Fig. 34, and page 147, Fig. 47),—it is obvious that I essentially agree with those observers who have maintained a direct transformation of the protoplasm into basis-substance. I assert, in entire accord with Max Schultze and Lionel Beale, that every territory originates from coalescence of protoplasmic bodies—plastids.

If we recall the fact (see page 133) that the basis-substance of a number of tissues is traversed by a delicate reticulum of living matter, we can realize that in the process of the formation of a tissue no living matter, certainly not all of it, perishes, but that it merely becomes invisible in the portions infiltrated with basis-substance.

If we, furthermore, recall the fact (see page 46) that the protoplasma itself goes through phases of development, we can also realize that the living matter appears in varying groups and

* "Zeitschrift f. Wissenschaftliche Zoologie." Bd. iii.
† "Müller's Archiv." 1857.
‡ "Cellular Pathologie," 1. Aufl., 1858.
§ "Studien des Physiolog. Institutes zu Breslau," ii. 1863.

accumulations—viz.: as a compact lump, as a nucleated body (plastid), or as a reticulum infiltrated with basis-substance.

It is not proved that the living portion of protoplasma is really ever changed into basis-substance; I have discovered the living matter, just as seen in medullary tissue, in places in which the

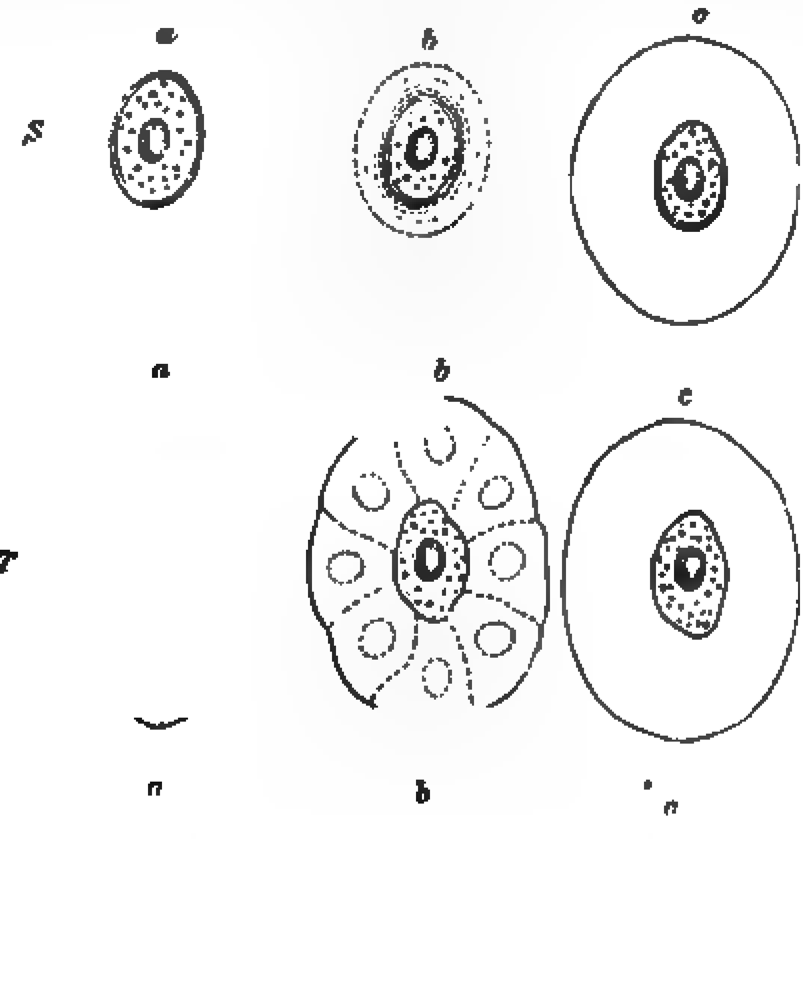


FIG. 71.—DIAGRAMS OF THE DEVELOPMENT OF CONNECTIVE TISSUE.

S, diagram of the *secretion theory*: *a*, the embryonal cell; *b*, the cell enlarged and its periphery transformed into basis-substance; *c*, the cell in middle of the considerably augmented basis-substance. *T*, diagram of the *transformation theory*: *a*, a number of medullary corpuscles, grouped in the shape of the future territory; *b*, the peripheral portion of protoplasm transformed into basis-substance, *c*, the cell in middle of basis-substance, sprung from a transformation of the peripheral protoplasm. *B*, diagram of the *bioplasson theory*: *a*, a number of plastids grouped in the shape of the future territory, all being reticular in structure and interconnected; *b*, the plastids coalesced, of the peripheral ones only the nuclei left, *c*, the formation of basis-substance accomplished, the central free plastid being the connective-tissue corpuscle, with coarse and delicate offshoots into the basis-substance.

protoplasm was formerly thought to have perished; nor is there any necessity, indeed, to assume that the basis-substance is a product of the living matter; for it may just as well be held that *nothing but the liquid originally filling the meshes of the living reticulum is transformed into basis-substance.*

In this case, we have simply to assume that solution or liquefaction of an already formed basis-substance sets free the living matter, and that the new grouping into lumps and elements (plastids) depends upon the formation of a new basis-substance in the mesh-spaces. This newly formed basis-substance will look striated or fibrous if the groups be spindle-shaped, such as in tendon and young bone-tissue; it will be ribboned if the groups be flat plates, such as in periosteum; it will appear lamellated should the groups be lenticular bodies, such as in bone-tissue; or, lastly, it will become globular with the formation of globular masses, such as in hyaline cartilage.

Within the basis-substance, the reticulum of living matter and the central portion of the protoplasma, the "cell," or "plastid," *remains intact.* From the central corpuscle the reticulum emanates, according to the shape of the unit of the tissue, either in a prevailing bipolar, or rectangular, or uniformly radiating direction. The forms of the fields of basis-substance will necessarily be determined by the main directions in which the living matter is distributed. The formation of basis-substance seen in that of a territory is illustrated in Fig. 71.

In order to elucidate in accord with the new views the formation of a fibrous basis-substance, we must consider the fact that one territory may contain *several* plastids interconnected. If each of the plastids, including those sharing in the formation of basis-substance, become elongated and split into delicate spindles, the result will be a large spindle- or rhomb-shaped territory, composed of numerous delicate spindles, which coalesce into fibrillæ, between which remain elongated plastids unchanged. As mentioned before (page 158), each fibrilla in reality is composed of a number of delicate spindles. Between the territories a larger number of plastids is left, and the blood-vessels take their course; or a more solid fibrous reticulum is developed, inclosing the territories, as, f. i., in myxomatous connective tissue.

The gradual development of basis-substance, therefore, admits of the following analysis:

In medullary tissue, a single plastid, or a small number of such, is converted into myxomatous basis-substance without the formation of territories;

In reticular tissue, a single plastid, or a small number of such, changes into myxomatous basis-substance, the territories of which are separated by a reticulum of plastids or fibers. The plastids within the territory remain unchanged in the lymph-tissue;

In the umbilical cord, a large number of plastids coalesce into territories of a partly myxomatous, partly fibrous, basis-substance, and these territories are separated by a broad reticulum of plastids, the "stellate mucoid-cells";

In fibrous connective tissue, each bundle is the result of coalescence of plastids much elongated and split up, and is composed of one or a number of territories, in which remain the connective-tissue corpuscles. A large number of plastids is left between the bundles;

In tendon, each bundle is a large territory containing a number of plastids arranged in chains, with numerous smaller bundles between them;

In periosteum, the plastids have flattened out so as to build up a rhomboidal ribbon, with a number of unchanged plastids, each ribbon being composed of one territory or of a number of them;

In the cornea, the flattened bundles or ribbons have coalesced into layers, traversed by the cornea corpuscles; each lamella is a flattened-territory, and between the territories are plastids similar to those within.

Between the groups, composed of plastids in many instances, and at an early stage of development, a very dense basis- or cement-substance appears. This is the "elastic tissue," seen in the periosteum in the shape of narrow plates or strips at the borders of the ribbons and their constituent fields. In the finished tissue, the elastic strips in varying amount border one or several territories, sometimes even smaller fields in one territory. The glue-yielding basis-substance, formed later, is by no means as dense and resistant as the first-formed elastic substance. This is proved by observations in inflamed periosteum. The basis-substance, however, is densified and made resistant, not only at the borders of the territories, but also around the cavities containing the plastids. This is the case in fibrous connective tissue as well as in cartilage- and bone-tissue.

The so-called "elastic tissue" is evidently no tissue sui generis, but a basis- or cement-substance, of an early formation and of considerable density. It arises from plastids, just as the glue-yielding basis-substance proper.

(3) Cartilage Tissue.

*History.** From the earliest time of histology to the present, true cartilage, such as the thyroid cartilage, has been looked upon as one of the simplest

* Written by Louis Elsberg: "Contributions to the Normal and Pathological Histology of the Cartilages of the Larynx," Archives of Laryngology, vol. ii., 1881.

tissues. To distinguish it from other kinds of cartilage, in which either a fibrous or a reticular aspect has been recognized, it is called hyaline, *i. e.*, resembling glass. The description of its structure by Meckauer, in 1836,* is essentially as that by Klein in 1880,† viz.: that it consists of a firm homogeneous basis-substance, in which are imbedded numerous small cartilage corpuscles. Meckauer wrote before the cell-doctrine, which has exercised so powerful an influence upon the medical mind, had been thought of. Indeed, that doctrine itself, as its founder, Schwann,‡ has recorded, was based to a large extent upon investigations of the constitution of cartilage. After J. Müller had described cartilage corpuscles that were hollow, and Gurlt had spoken of some as vesicles; when Schwann had succeeded, as he thought, "in actually observing the proper wall of the cartilage corpuscles, first in the branchial cartilages of the frog's larvæ, and subsequently also in the fish," he was led by these and other researches to conjecture "that the cellular formation might be a widely extended, perhaps a universal, principle for the formation of organic substances."

Schwann considered that the cartilage corpuscles, or cartilage cells, as they were thenceforth called, are imbedded in a matrix which is capable of producing the cells, and which he therefore called cytoblastema. Goodsir, Naegeli, and finally Virchow advanced the histology of cartilage in so far as they claimed that the cartilage cells cannot possibly arise from the matrix or intercellular substance. Even Virchow adhered, however, to the idea of Schwann, that the cartilage cell is a vesicle filled with a more or less transparent fluid, in which is suspended the nucleus; and, although he was aware of the life of the cell in general, nothing was suggested by him as to the life of cartilage. It is true, Donders and H. Meyer had observed that the cells of hyaline cartilage were capable of proliferation; § nevertheless the idea became prevalent, more perhaps from implication—because, on account of the absence of blood-vessels, it was believed not liable to inflammation—than from any direct statement to that effect, that cartilage was devoid of life. The vitality of cartilage corpuscles was made clearly probable by the observation of the effect of electrical shocks upon them, by Heidenhain, ‖ and by Rollett,¶ and the investigations of Reitz,[1] Boehm,[2] Hutob,[3] and Bubnoff,[4]—investigations which except Boehm's, were made under Stricker; it was proved positively by Heitzmann in 1873.[5]

With the question whether or not the so-called cartilage cell is alive,

* "De Penitiori Cartilaginum Structura Symbolæ." Diss. anat.-phys., auctore M. Meckauer, M. D. Breslau: Schultz & Co., 1836, tab. 4, p. 16.

† "Atlas of Histology." London: Smith, Elder & Co., 1880, p. 48.

‡ "Mikroskopische Untersuchungen über die Uebereinstimmung in der Structur und dem Wachsthume der Thiere und Pflanzen," von Dr. Th. Schwann. Berlin: G. E. Reimer, 1839, p. 270. "Microscopical Researches into the Accordance in the Structure and Growth of Animals and Plants." Translated by Henry Smith. London: Sydenham Society, 1846. Introduction.

§ Mueller's "Archiv für Anatomie," 1846.

‖ "Studien aus dem Physiologischen Institut zu Breslau," ii. Heft, 1863.

¶ Stricker's "Handbuch der Lehre von den Geweben," Article, "Knorpelgewebe," 1868.

[1] "Sitzungsber. der K. Akademie der Wissensch. in Wien," Bd. 55, 1867.

[2] "Beiträge zur Normalen und Pathologischen Anatomie der Gelenke." Inaug. Dissertation, Würzburg, 1868.

[3] "Untersuchungen über Knorpelentzündung." Wiener Med. Jahrbücher, 1871, p. 399.

[4] "Beiträge zur Kenntniss der Structur des Knorpels." Sitzungsber. der K. Akad. d. Wiss. in Wien, Bd. 57, 1868.

[5] "Das Verhältniss zwischen Protoplasma und Grundsubstanz im Thierkörper." Sitzungsber. der K. Akad. d. Wien; Wien, Bd. 67, 1873, and Wiener Med. Jahrbücher, 1873.

another question arose, viz.: how can so isolated a corpuscle (imbedded in a firm "intercellular" substance) obtain nutrition? It was assumed that the nourishing liquid reaches the corpuscle either by diffusion or else through canals, or clefts, or fissures in the homogeneous basis-substance. The idea of the existence of juice-channels originated with Von Recklinghausen. He found in silver-stained preparations of the cornea communicating colorless spaces on a dark background, and believing that the cornea consisted of fibrillary tissue knit together by a cement-substance, he thought that this cement-substance was tunneled by a system of communicating canals, "Saft-Kanälchen," and that it is this system of canals which is not stained by silver. Innumerable investigations, under all sorts of circumstances, have been undertaken to settle satisfactorily whether preformed juice-channels exist in cartilage, or whether juices can be imbibed without such. In lower animals corresponding canals had long been reported to be found, by Queckett * and by Bergmann † in cephalopodes, and by Leydig ‡ in various fishes; and certain pathological observations by Virchow, § Zahn, ‖ Cornil and Ranvier, ¶ and Rindfleisch,[1] as well as senile changes studied by Weichselbaum,[2] seemed to point to their presence in man. Pigment particles were introduced into the circulation, in the hope of discovering the manner in which they penetrate the tissue of cartilage, by Gerlach,[3] Maas,[4] Arnold,[5] and Nykamp and Treub[6]; Küttner, with the same end in view, introduced solutions into the trachea and examined the bronchial and tracheal cartilages[7]; and Hénoque,[8] Budge,[9] Tizzoni,[10] and others forcibly injected liquids as well as solid particles into the tissues. The results of these experiments, and of examinations with various re-agents, are contradictory of each other. For instance, while Bubnoff,[11] Hertwig,[12] Hénoque,[13] Lœwe,[14] Thin,[15]

* "Catalogue of the Historical Series in the Museum of the Royal College of Surgeons," 1850, vol. i., p. 102.

† "Disquisitiones Microscopicæ de Cartilaginibus in specie Hyalinicis." Inaug. Dissert., Dorpat, 1850.

‡ "Zur Anatomie und Histologie der Chimæra Monstrosa." Mueller's Archiv, 1851, p. 242.

§ "Ein Fall allgemeiner Ochronose der Knorpel und knorpelähnlichen Theile." Virchow's Archiv, xxxvii., 1866, p. 212.

‖ "Ueber Pigmentinfiltration des Knorpels." *Ibid.*, lxxii., 1878.

¶ "Manuel d'Histologie Pathologique," Paris, 1869, p. 427.

[1] "Lehrbuch der Pathologischen Gewebelehre." Leipzig, 1878, p. 553.

[2] Sitzungsber. der K. Akademie d. Wiss. in Wien, Bd. 75, 1877.

[3] "Ueber das Verhalten des indigschwefelsauren Natrons im Knorpelgewebe lebender Thiere." Erlangen, 1876.

[4] "Ueber das Wachsthum und die Regeneration der Röhrenknochen." Archiv für klinische Chirurgie, xx., 1877.

[5] "Die Abscheidung des indigschwefelsauren Natron im Knorpelgewebe." Virchow's *Archiv*, lxxiii., 1878.

[6] "Beitrag zur Kenntniss der Structur des Knorpels." Archiv für Mikroskop. Anatomie, xiv., 1877.

[7] "Die Abscheidung des indigschwefelsauren Natron in den Geweben der Lunge." Centralblatt f. d. Med. Wiss., 1875, No. xiii., p. 268.

[8] "Structure des Cartilages." *Gazette Médicale*, 1873, p. 589; p. 617.

[9] "Die Saftbahnen im hyalinen Knorpel." Archiv für Mikroskop. Anatomie, xiv., 1877; xvi., 1879.

[10] "Sulla Istologia Normale e Patologica delle Cartilagini Ialini." Archivio per le Scienze Mediche, ii., 1877. [11] *Loc. cit.*

[12] "Ueber die Entwickelung und den Bau des elastischen Gewebes im Netzknorpel." Archiv für Mikroskop. Anatomie, ix., 1873, p. 80. [13] *Loc. cit.*

[14] "Ueber eine eigenthümliche Zeichnung im Hyalinknorpel." Wiener Med. Jahrbücher, 1874.

[15] "On the Structure of Hyaline Cartilage." *Quarterly Journal of Microscopical Science*, vol. xvi., 1876.

Ewetzky,* Petrone,† Budge,‡ Nykamp,§ Fürbringer,‖ and a number of others consider the existence of canals in the basis-substance of cartilage proved by their experiments and treatment of their preparations with silver nitrate, gold chloride, hyperosmic acid, chromic acid, ammonia bichromate, etc., etc.; investigations by exactly the same means have convinced Sokolow,¶ Retzius,[1] Colomiatti,[2] Brückner,[3] Toldt,[4] Genzmer,[5] Gerlach,[6] Tillmanns,[7] Tizzoni,[8] and others, of just the contrary; and there is a third party which believes, with Arnold,[9] that the basis-substance is made up of fibrillæ, that there are delicate fissures between the fibrils, that these fissures penetrate the capsule, and that "the nutrient material passes through these interfibrillar and intracapsular fissures into the pericellular space." Flesch, the latest writer on the subject, adds[10] that these fissures need not necessarily be, and in fact are not, empty, but that they are occupied by the interfibrillar cement-substance, which, being of a "viscous soft" *(zähweich)* material, permits the imbibition and conveyance of the nutrient liquid.

It is claimed that hyaline basis-substance consists of fine fibrils, so closely held together by a cement-substance that the mass appears to be homogeneous. This idea, though not entirely novel, as the older anatomists seem to have had it,[11] has been brought forward by Tillmanns, and is doubtless original with him.[12] It is said that the interfibrillar cement-substance can be dissolved out by certain re-agents, and then the fibrillation seen under the microscope. According to the varying arrangement and interrelation of the fibrillæ, Tillmanns speaks of three types of cartilage tissue — viz., parallel-fibery, net-form, and lamellous. No doubt he saw under the microscope appearances which underlie the distinction which he thus made, but, unfortunately, he misinterpreted these appearances. Nevertheless, he has had followers. Thus, Baber reported[13] that, having undertaken to test the accuracy of Tillmanns' assertions, and not succeeding in finding the fibrillation.

* "Entzündungsversuche am Knorpel." Vorläufige Mittheilung, Centralblatt f. d. Med. Wiss., 1875, No. 16; "Untersuchungen aus dem Path.-anat. Institut zu Zürich," iii. Heft, 1875.

† "Sulla Struttura Normale e Patologica delle Cartilagine e degli Epitelii." Napoli, 1876.

‡ *Loc. cit.* § *Loc. cit.*

‖ "Ueber das Gewebe des Kopfknorpels der Cephalopoden." Morpholog. Jahrbücher, iii., 1877, p. 453.

¶ "Ueber den Bau des Nasenknorpels," etc., ref. Canstatt's Jahresbericht. 1870, p. 24.

1 "Bitrag till Kännedomen um Brusknäfnaden." Nord. Med. Arkiv, iv., 1872.

2 "Sulla Struttura delle Cartilagini Ialini e Fibroelastica Reticolata." Gazetta Cliniche di Torino, 1873, No. xxxii.; Rivista Clinica di Bologna, 1874, No. v.; Giornale della Acad. di Torino, 1876.

3 "Ueber Eiterbildung im Hyalinen Knorpel." Inaug.-Dissert., Dorpat, 1873.

4 "Lehrbuch der Gewebelehre." Stuttgart, 1874, p. 143.

5 "Ueber die Reaction des Hyalinen Knorpels," etc. Virchow's Archiv, lxii., 1875; Centralblatt f. Chirurgie, 1875, No. cxlvi.

6 *Loc. cit.*

7 "Beiträge zur Histologie der Gelenke." Archiv für Mikroskop. Anatomie, x., 1874, pp. 354, 435.

8 *Loc. cit.* 9 *Loc. cit.*

10 "Untersuchungen über die Grundsubstanz des hyalinen Knorpels." Würzburg: Stuber, 1880.

11 See: Wm. Hunter "On the Structure and Diseases of Articular Cartilages," Philosophical Transactions, vol. xlii., p. 514, London, 1742-43; M. de Làsone, "Second Memoire sur l'Organization des Os," Mem. de l'Academie Roy. des Sciences, tome lxix., Paris, 1752; more recently, also, Hoppe, Virchow's Archiv, v., p. 175.

12 *Loc. cit.*, p. 401; and "Ueber die fibrilläre Structur des hyalinen Knorpels." Archiv f. Anatomie u. Physiologie, Anat. Abth., 1877, p. 9.

13 "On the Structure of Hyaline Cartilage." *Journal of Anatomy and Physiology*, vol. x. Part I., October, 1875.

although he had followed Tillmanns' method of maceration, he accidentally made momentary pressure on the glass cover and thereupon obtained satisfactory proof of the fibrillar constitution of the basis-substance. Reeves * has also convinced himself of the existence of normal fibrillation in human cartilage. Ziegler seems to have done the same; † and Flesch regards it as a matter beyond question. He speaks of it as "generally known and most easily demonstrable." ‡ Furthermore, he thinks that some portions, or perhaps layers, of the basis-substance are more compact than others, and that this may also account for the facility of cleavage in determinate directions.

Leidy insisted § that the basis-substance of hyaline cartilage has a peculiar filamentous structure, but his interpretation, that the granular filaments run simply parallel to each other, does not cover the truth, and has not attracted any attention. With the exception of Leidy, however, no one, until nine years ago, seems to have questioned the homogeneousness of the mass of basis-substance in which the separate corpuscles were supposed to be imbedded. In 1872, Heitzmann ‖ first proved the presence of a net-work structure in the basis-substance. Somewhat similar appearances had previously been more or less vaguely described, but not properly interpreted or appreciated, by Remak, ¶ by Heidenhain,[1] by Broder,[2] by Frommann,[3] and possibly by others.

After Heitzmann, Hertwig[4] observed processes of living matter penetrate the basis-substance of reticular cartilage; and Colomiatti stated[5] that he had failed to find cell offshoots in hyaline cartilage, either after treatment with gold or silver or *in vivo*, although he had seen cartilage-cell offshoots in other than hyaline cartilage.

I have had the opportunity to repeat Heitzmann's investigations under his own eye and with his assistance, but the results as to their correctness at which I arrived were, to the best of my belief, uninfluenced by him. I reported in 1875[6] that I had seen the net-work structure in the corpuscles of hyaline cartilage, in the nucleus and in the basis-substance, exactly as Heitzmann had described it two years previously.[7]

In January, 1876, Thin's memoir was published,[8] in which he reported that, in particular preparations, he had seen "fine glistening fibers enter the cartilage substance, into which, however, he has not been able to follow them." Again: "The ordinary granular protoplasmic cells of hyaline cartilage are analogous, according to the views of the author, to the stellate

* "On the Structure of the Matrix of Human Articular Cartilage." *British Medical Journal*, Nov. 11, 1876, p. 616.

† Bericht der 50. Naturforsch. Versammlung zu München, 1877.

‡ *Loc. cit.*, p. 74.

§ "Proceedings of the Academy of Natural Sciences of Philadelphia," vol. iv., No. 6, 1848; and *American Journal of Medical Sciences*, April, 1849, p. 282.

‖ "Wiener Medizin. Jahrbücher," Heft iv., 1872.

¶ "Ueber die Entstehung des Bindegewebes und des Knorpels." Archiv für Anatomie, 1852, p. 63, *et seq.*

[1] *Loc. cit.*

[2] "Ein Beitrag zur Histologie des Knorpels." Dissert., Zürich, 1865.

[3] "Untersuchungen über die normale und pathologische Anatomie des Rückenmarkes." II. Theil. Jena, 1867, pp. 29, 30.

[4] *Loc. cit.*

[5] *Loc. cit.*

[6] "Transactions of the American Medical Association," vol. xxvi., 1875, pp. 163, 164.

[7] "Untersuchungen über das Protoplasma. II. Das Verhältniss zwischen Protoplasma und Grundsubstanz im Thierkörper." Sitzungsber. d. K. Akad. d. Wissensch. in Wien, lxvii., May, 1873.

[8] It is dated August, 1875, *loc. cit.*

cells of the cornea and connective tissue generally." Thin obtained, by silver-staining, appearances similar to Heitzmann's, but unfortunately misinterpreted them.

In 1879, Spina reviewed the subject.* He accorded to Heitzmann the merit of the discovery, but as in the intervening seven years I alone had publicly corroborated it, and he was not aware of that corroboration, he thought that "the existence of cells with solid offshoots in genuine hyaline cartilage is not definitely proved," and undertook to settle the question. After many fruitless attempts, he found out a method of examination "by which ramifying cells in hyaline cartilage can be demonstrated, not only with ease, but also with certainty." The method and the results, as he has described them, are as follows: "The cartilage, best the articular ends of bones, is placed into alcohol for three or four days; then the sections are made and the examination is conducted in alcohol. From such specimens positive proof is obtained that the cells of hyaline cartilage have solid offshoots. These offshoots emanate mostly from the body of the shriveled cells, penetrate the basis-substance, and inosculate with offshoots of other cells. Their number and thickness are subject to numerous variations. . . . The cell offshoots do not, as a rule, ramify. . . . Examination with powerful immersion lenses (Hartnack, No. 15) teaches positively that the cell offshoots not only pierce the capsule, but that the capsule extends also to the offshoots themselves, so that at their origin they are surrounded, like the cell body, by a wall. . . . Upon adding a drop of glycerine to the alcohol specimen, or on staining it after one of the usual methods, the cell offshoots disappear more or less rapidly; hence, it is clear that the hyaline, structureless aspect of the cartilage basis-substance is really due to the methods of preparation hitherto in use, while, when examined in alcohol, as above described, the cell offshoots invariably become visible." He added that he had succeeded a few times in seeing—faintly only, it is true—the same structure in living hyaline cartilages. On incorporating, for a sufficient length of time, carmine into the body of frogs, Spina found cartilage corpuscles of which the nuclei, the body, and the offshoots had taken in some of the coloring matter. As the offshoots disappeared and the carmine granules seemed to lie in the hyaline basis-substance when a drop of glycerine was added, it is easy to see how previous investigators came to be misled into supposing the coloring matter to have passed into the hyaline substance and into interfibrillar fissures. With excessive caution, Spina adds: "Whether they (the coloring particles) can also move along outside of the cell offshoots has not yet been proved."

In the same year Prudden,† and, in 1880, Flesch,‡ also described cilia-like processes of cartilage corpuscles; and the latter admitted that in exceptional cases he had succeeded in tracing them more or less distinctly into the basis-substance.

Varieties of Cartilage Tissue. Cartilage is a very dense, opaque, and highly elastic tissue, the basis-substance of which is not strictly gelatinous, as on being boiled it yields a cloudy,

* "Ueber die Saftbahnen des hyalinen Knorpels." Sitzungsber. der K. Akad. d. Wiss. in Wien, lxxx., Abth. iii., November, 1879.

† "Beobachtungen am lebenden Knorpel." Virchow's Archiv, lxxv., 1879, p. 185.

‡ *Loc. cit.*, pp. 59-63.

coagulating liquid, which has an odor similar to that of glue, but is not viscid. The reticulum of living matter is infiltrated with this so-called "chondrogenous" basis-substance, the cavities of which hold plastids varying greatly in size, number, and configuration. In the juvenile condition of the individual, the plastids are generally solid and homogeneous; in the middle-aged they are distinctly nucleated, exhibiting a very fine reticulum of living matter. That these plastids in the living tissue are alive, I was the first to demonstrate (page 116). Cartilage, as well as other varieties of connective tissue, should be preserved in a solution of chromic acid; to examine fresh cartilage kept in pure water is very objectionable, as in this liquid the plastids soon become vacuoled and destroyed.

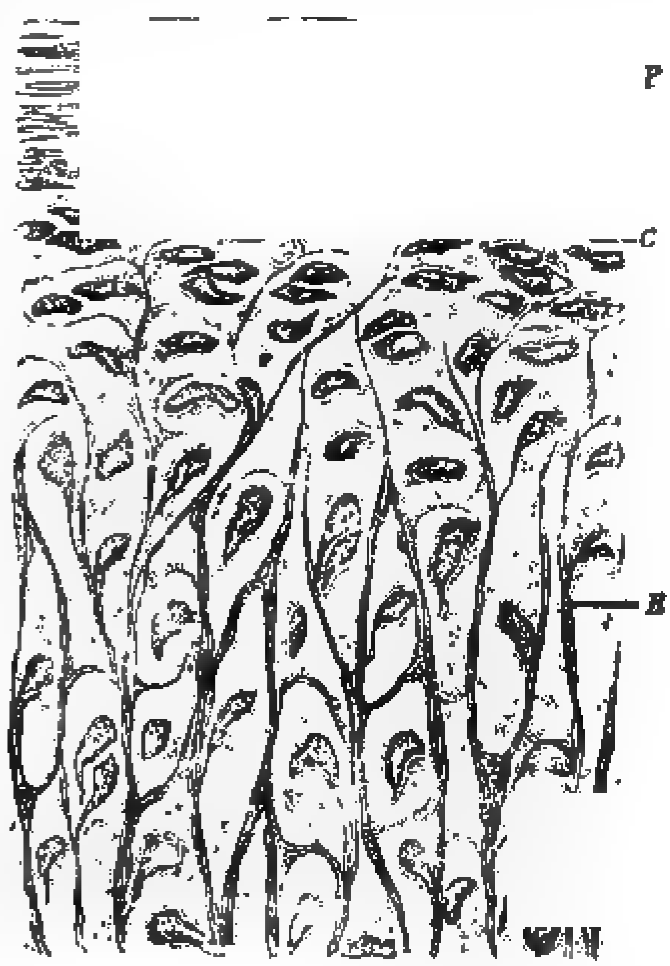


FIG. 72.—RETICULAR CARTILAGE FROM THE EPIGLOTTIS OF A CHILD. CHROMIC ACID SPECIMEN.

C, hyaline cartilage traversed by fibers, *E*, in a reticular arrangement; the reticulum surrounds the territories of the cartilage corpuscles; *P*, perichondrium. Magnified 500 diameters.

We distinguish three varieties of cartilage, which may be arranged according to the order in which they approach the structure of fibrous connective tissue: reticular or elastic cartilage; fibrous or striated cartilage; hyaline cartilage.

(a) Reticular or Elastic Cartilage resembles the reticular variety of myxomatous connective tissue. The difference is that its basis-substance, instead of being mucous, is dense and chondrogenous, and is traversed in an apparently irregular manner by very dense, bright, elastic fibers. Owing to the presence of this elastic reticulum, the tissue has a yellowish color and a high degree of pliability. (See Fig. 72.)

The elastic fibers, as a rule, are very delicate, and sometimes are packed closely together in slender bundles, their width vary-

ing greatly in different animals. Sometimes they run parallel with each other, sometimes they interlace in different directions. They are coarser in the middle portions of the tissue, and gradually grow thinner as they approach the periphery; here they often blend with the adjacent fibrous connective tissue of the perichondrium. Not infrequently we see at the points of intersection of the elastic reticulum slender oblong nuclei, which is a positive proof that the elastic fibers have originated from branching plastids found between the territories of the cartilage corpuscles.

The meshes of the elastic reticulum contain a chondrogenous basis-substance, and usually in the middle of each mesh one or two cartilage corpuscles can be distinguished. In young individuals these corpuscles are either homogeneous and shining, or composed of coarse, bright granules and destitute of nuclei. They are more bulky in the middle of the plate of the reticular cartilage, and become flattened toward the perichondrium, where they undergo a gradual but rapid change into the spindle-shaped corpuscles of the perichondrium. Some of the cartilage corpuscles are pear-shaped, and unite by means of slender, stem-like offshoots with the elastic reticulum. Their periphery is everywhere thorny, which indicates that their structure, as well as that of the chondrogenous and elastic basis-substance, is identical with that of all other connective-tissue formations.*

Little is known regarding the senile changes of this tissue. It is asserted that in persons of middle and advanced age the elastic cartilage of the auricle of the ear becomes fibrous, and H. Müller has observed calcification and ossification in auricles of dogs.

According to O. Hertwig, the first development of the elastic fibers takes place in the shape of extremely delicate fibrillæ, as the result of the "formative activity of the cartilage cells" in their most peripheral portions. The further growth, he says, is the result of "intussusception," independently of the cartilage corpuscles. I consider the development of reticular cartilage to be the same as that of the reticular myxomatous tissue. Territories are formed by coalescence of embryonal plastids, in which

* As a matter of curiosity, it is worth mentioning what method A. Rollett ("Manual of Histology," by S. Stricker, American edition, 1872) recommends for obtaining the best specimens of reticular cartilage. "Boil the auricle of the ear of man for a short time, dry it, and finally make sections of these boiled mummies."

ıe or two plastids remain as unchanged cartilage corpuscles. t the periphery of the territories, branching plastids form, givıg rise to the elastic reticulum. The whole of the basis-substance emains traversed by a delicate reticulum of living matter.

Reticular cartilage is met with in a few places only—the aurie of the ear, the wall of ıe external auditory canal, ıd of the Eustachian tubes, ıe epiglottis, and the smallst cartilages of the larynx, ıcluding the vocal process f the arytænoid cartilages. he tarsus of the eyelids, hich was formerly considred cartilaginous, is now nown to be constructed of very dense fibrous conective tissue, richly supied with branching plasds.

(b) Striated or Fibrous artilage. There is scarcely ıy reason for considering ıis tissue to be *sui generis*, s it is invariably mixed ith hyaline cartilage, ther in its interior or t its peripheral portions, here fibrous cartilage esıblishes the connection etween hyaline cartilage nd fibrous connective tisıe. Fibrous cartilage, ıerefore, blends with both ıe last-named tissues, and epresents a stage of tranıtion of one into the other.

H

F

FIG. 73.—STRIATED OR FIBROUS CARTILAGE FROM THE CONDYLE OF FEMUR OF A RABBIT, EIGHT MONTHS OLD. SAGITTAL SECTION, NEAR THE LATERAL SURFACE OF THE CONDYLE. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

Transition of hyaline cartilage, *H*, into fibrous cartilage, *F*. Magnified 800 diameters.

ts basis-substance is glue-yielding and composed of delicate brillæ, usually without a definite formation of bundles, while ıe plastids are large and nucleated, either regularly scattered or rranged in chain-like rows. (See Fig. 73.)

According to C. Toldt, we meet with fibrous cartilage in the

interarticular and intervertebral disks; in the cartilaginous projections (labra cartilaginosa) of concave articular surfaces, and in those portions of the tendons which glide over bones. In the latter instance, the cartilage corpuscles extend far into the tissue of the tendon. In the intervertebral disks of middle-aged persons, the upper and under portions consist of a tissue closely resembling hyaline cartilage, with flat lenticular corpuscles; from this layer arise the bundles of fibrous cartilage interwoven in oblique direction. The bundles are thinner near the center, and increase in size from within outward. The most central portion of the disk is non-striated, of uniform appearance, and of a gelatinous consistence, approaching, therefore, the features of myxomatous basis-substance; it is abundantly supplied with plastids arranged in nests, like cartilage corpuscles. The lateral portions of the disks consist of a dense fibrous connective tissue, likewise blending with the fibrous cartilage.

The fibrous tissue which we find within hyaline cartilage, mainly that of the ribs, the tracheal and laryngeal cartilages, but not in normal articular cartilages, is of considerable interest. Histologists claim that this fibrous tissue is a product of secondary or senile changes, occurring very regularly, some say between the fifth and sixth, others between the tenth and twelfth, year of life. A queer senile metamorphosis, indeed, which is of regular occurrence in childhood.

L. Elsberg has observed in specimens of the thyroid and cricoid cartilages of human fœtus, five to six months old, a delicately striated basis-substance in the middle of the cartilaginous plates. This striation becomes more distinct with the age of the individual, and sometimes even in middle life invades nearly all the laryngeal cartilages. The same change has been observed in articular cartilages of so-called arthritic persons. The most peripheral portions of the cartilage, as a rule, remain free of fibrous metamorphosis. The fibers are arranged in either straight or slightly curved bundles, and exhibit features identical with those of the lateral surfaces of the condyles, illustrated in Fig. 73.

We must abandon the opinion that this fibrous tissue is the result of a senile metamorphosis. The question remains unsettled, however, whether hyaline basis-substance of cartilage is directly changed into fibrous, or whether this transition goes on through the intermediate stage of medullary tissue, in accordance with the general rule of tissue transformation.

(c) Hyaline Cartilage. The name implies that the dense basis-substance of this tissue is transparent and devoid of any trace of structure. This is true only of cartilage specimens mounted in balsam or varnish, such as were formerly used for observation. Both in fresh specimens and in those preserved in chromic acid, the basis-substance, even with moderate powers of the microscope, is not hyaline, but of finely granular appearance.

The basis-substance contains cavities, in which lie the plastids, termed cartilage corpuscles. Around the cavities the basis-substance is often concentrically striated. This feature led to the supposition that cartilage corpuscles were inclosed in "capsules." The capsules are nothing but the optical expression of different degrees of densification, found in all other varieties of connective tissue. Condensed basis-substance in the form of a capsule may occur around single cartilage corpuscles or around corpuscles grouped together, and frequently such capsules are altogether absent. Their production is closely connected with the formation of territories during development, and their power of resistance can be proved by long-continued boiling, especially in acidulated water.

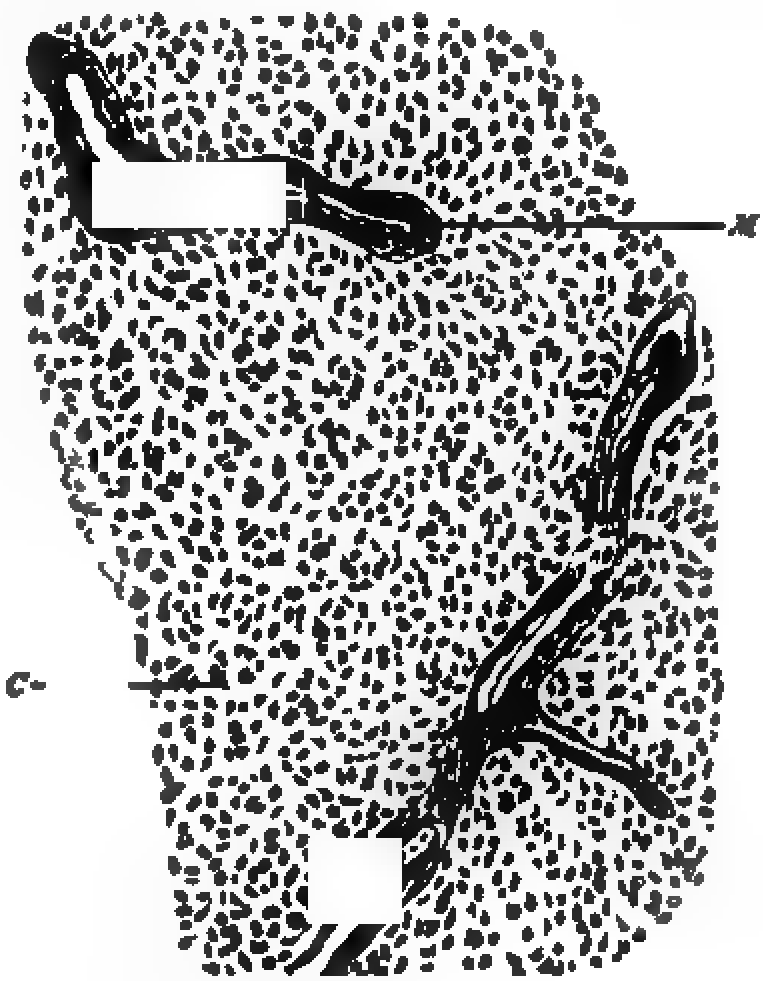


FIG. 74.—HYALINE CARTILAGE FROM THE CONDYLE OF FEMUR OF A NEW-BORN PUP. CHROMIC ACID SPECIMEN.

C, the tissue of the hyaline cartilage, with scattered groups of cartilage corpuscles; M, Medullary spaces, containing blood-vessels and medullary tissue. Magnified 100 diameters.

Hyaline cartilage, when fully developed, is scantily supplied with blood-vessels; large masses of the tissue are met with which are entirely destitute of vessels. Undeveloped, embryonal cartilage, however, is traversed by a relatively large number of medullary canals, in which a complete system of blood-vessels—

arteries, veins, and capillaries—is found, besides a certain amount of medullary tissue, filling the space between the blood-vessels and the walls of the canals. The medullary canals, according to C. Langer, appear in the epiphyseal cartilage of shaft-bones (femur) after the third month of embryonal life. These canals are all in connection with the outer fibrous investment of the cartilage—*i. e.* the perichondrium, from which the blood-vessels enter the canals. The vascular medullary spaces decrease with the age of the individual, although a few such spaces have been traced up to the thirtieth year of life (Bubnoff). They are in intimate relation with both the progressive and regressive development of cartilage. (See Fig. 74.)

The cartilage corpuscles are never scattered uniformly throughout the basis-substance, but always massed together, and the amount of basis-substance between the different members of a group of corpuscles is less than that which surrounds the groups. The groups vary in their general form in different portions even of the same cartilage. In epiphyseal cartilage of young animals, the corpuscles are arranged in flat groups around the articular surface; they produce more or less globular or elongated clusters in the middle portion, and on approaching the diaphysis they are arranged in elongated rows. In a sagittal (antero-posterior) section through such an epiphyseal cartilage, the corpuscles appear oblong or spindle-shaped along the articular surface, which indicates that their broadest diameter runs parallel with the outer surface. In the middle portion they are more or less globular. Near the diaphysis they again become discoid, appear flattened, oblong, or spindle-shaped if cut in a sagittal direction, and circular in a direction vertical to the shaft of the bone.

With higher powers (300–500) of the microscope we recognize that, especially in the middle portions of cartilaginous formations, some corpuscles not infrequently lie very close to each other, so as to mutually flatten their proximal surfaces. Between so-called twin formations there is either a very narrow light rim or a somewhat broader layer of basis-substance, and if an entire group of corpuscles exhibit such twin formations (seen most distinctly in the cartilage of the trachea), the narrow frame between the corpuscles in its regular arrangement presents a very pretty appearance. These double formations have been considered, for the last twenty years or more, proofs of the division of cartilage cells. This is a very mistaken idea, for it is impossible to under-

stand how corpuscles imbedded in a dense and tough basis-substance could enlarge and divide — cartilaginous tissue itself, moreover, being perhaps the most inactive of all tissues. These multiple bodies cannot be the products of a division, as they are obviously formed simultaneously with the cartilage, and correspond to the double or treble, etc., corpuscles so often seen in the territories of other varieties of connective tissue. They cannot alter, unless the dense basis-substance around them is liquefied, or they themselves are transformed into basis-substance.

Hyaline cartilage is a very common tissue in the body, and is found in an amount varying with the age of the individual. At a certain period of embryonal development, the entire skeleton is composed of hyaline cartilage, and from this is developed the whole osseous system, with the exception of the flat skull-bones. In the fully developed body this cartilage constitutes all articular surfaces of the bones, the anterior portions of the ribs, and the frame of the nose, the larynx, the trachea, and the bronchi.

The articular cartilage is covered with a single, often indistinct, endothelial layer on the gliding surfaces, and surrounded by a richly vascularized delicate fibrous connective tissue — the synovial membrane — on the lateral surfaces. All other formations of hyaline cartilage are invested by a layer of a dense fibrous connective tissue, the perichondrium, holding numerous blood-vessels, and in its construction more or less identical with that of the periosteum (see page 124). A distinct boundary-line between cartilage and perichondrium does not exist, as a gradual transition of the hyaline into the fibrous basis-substance takes place, and the cartilage corpuscles, which are always flattened near the surface, blend with the oblong or spindle-shaped plastids of the fibrous connective tissue.

Hyaline cartilage is prone to secondary changes. The solid constituents increase with advancing age. According to E. Von Bibra, the ash-remnants of the cartilage of ribs of man continually increase with advancing age to such a degree that, while the solid remnants of a child six months old were only 2.29 per cent., those of a man forty years old were 6.1 per cent. Even in middle age, many of the cartilage-corpuscles contain fat-granules, which often coalesce into fat-globules, replacing to a certain extent the living matter. Granular depositions of lime-salts are often met with in the basis-substance of cartilage of the aged, especially in the ribs and the laryngeal cartilages. Sometimes

these are transformed into regular bone. The older a person grows, the less hyaline cartilage is found in his body.

Kölliker made the curious discovery of a "parenchymatous or cellular" cartilage, constructed wholly of cells, without any trace of basis-substance. Among others, the chorda dorsalis, a light line close above the earliest formation of the central nervous system in the embryo, is considered to be such a parenchymatous cartilage. Such a thing, however, is contrary to all we know of what could possibly be any variety of connective tissue. According to V. v. Mihalkovics, the chorda dorsalis is no cartilage at all, but a duplicature of the outer, epithelial germ-layer (Toldt). If this be correct, it would be another instance of an epithelial elongation which, after returning to the condition of an embryonal and medullary tissue, gave rise to connective-tissue formations. We know that this is the case with the thyroid body and the enamel-tissue of the teeth.

The Structure of Hyaline Cartilage.*

Fresh, articular cartilage is a suitable object for the study of the histology of hyaline cartilage. If we place a thin section, to which is added a drop of one-half per cent. solution of common table-salt, under the microscope, with an immersion lens No. 10, we will find a number of details heretofore overlooked. The following description is a study of a specimen taken from a horizontal section of the condyle of femur of a young, full-grown dog; it answers to the corresponding cartilages of the cat and the rabbit.

The bodies of the cells appear finely granular, bounded by a somewhat denser layer. The contour of the cartilage cell being accurately in focus, there appears between the cell and the basis-substance a light, very narrow rim, which is traversed by numerous extremely delicate, radiating, grayish thorns or streaks. All these thorns are conical, the broad base emanating from the body of the cell and the thin point directed toward the basis-substance. Wherever two cells lie close together, the light rim between them is pierced in a transverse direction by grayish threads.

When in the cell the nucleus is distinctly visible, its shape will be found to correspond to the shape of the cell-body, and in its finely granular interior the bright nucleolus will be usually apparent. A narrow light rim is found to surround the nucleus, which, on being sharply focused, shows radiating thorns, whose

* Translated from "Studien am Knochen und Knorpel." Wiener Medi. Jahrbücher, 1872.

emanate from the nucleus, and whose points blend with rotoplasma of the cell. These conical spokes are clearly d only when the light rim around the nucleus is distinct.

a carefully examining the basis-substance, a very delicate, t granular, conformation is recognizable, as if dark fields alternating with light ones, and in some places giving the ssion that the light fields formed ramifications, or even a te net-work.

'ith the knowledge that from the cartilage cells offshoots ate, and the basis-substance has an indistinct reticular for-

75.—Hyaline Cartilage from the Border of the Condyle of mur of a Young Dog. Transition into Fibrous Cartilage. 'ained with Nitrate of Silver. [Published in 1872.]

spaces with indistinct cartilage corpuscles, freely branching and connecting. *B*, dark n basis-substance, traversed by a light reticulum. Magnified 800 diameters.

n, and under the impression of pictures of inflamed carti- which will be dwelt upon later, I proceeded to stain the age with nitrate of silver.

prepared the articular extremity of the femur by removing uscles and severing the shaft at a certain distance above

the knee-joint, and in this way obtained the condyles, as it were, on a handle formed by the stump of the femur. After the synovia was washed off, I rubbed a stick of nitrate of silver for several minutes over the condyles, transferred the specimen to water, and exposed it to daylight. After a few days, the parts which had been brought in contact with the re-agent became dark brown. The most superficial layer was removed as useless, and the next layer was examined. I would remark that sections from deeper portions, which at first are but slightly tinted by the silver-salt, assume a deep color on exposure to daylight. The deeper layers of the condyle, too, are dyed brown, and to a certain depth are well adapted for new sections.

The following description is that of specimens taken from the condyles of a young and an old dog: they showed the same features.

From the stained specimens taken from the anterior and under portions of the condyle, I could obtain nothing satisfactory for establishing the idea of a reticular structure. As soon, however, as I reached the lateral surface, close to the edge, the aspect of things at once became changed. (See Fig. 75.)

The basis-substance at the borders of the cartilage cavities is stained dark brown, in other portions light brown-red. From the cavities of varying shapes light offshoots are thrown out in different directions, which may be grouped in three orders, according to their calibers. The broadest offshoots, those of the first order, either connect cartilage cavities, or run merely into the basis-substance. The somewhat narrower offshoots, those of the second order, project from either the cartilage cavities or the broader offshoots, and ramify freely into the very narrow ones, those of the third order. The latter shoot out from the cartilage cavities and the processes of the first and second order, as well as from the ends of coarser processes, and traverse the basis-substance throughout. Thus a rich, extremely delicate reticulum of light, irregular lines is produced, with numerous varicose enlargements, the meshes of which reticulum are filled with the brown basis-substance. In the cavities we recognize the dim, unstained cell-bodies, with their enlarged, thorny nuclei and their offshoots, which are traceable into the processes of the cavities of the first order.

In specimens taken from the anterior and under surface of the condyles, offshoots of the third, and occasionally some of the second, order are found, which are readily distinguished, wherever

the borders of the cartilage cavities are pierced by radiating light lines. The lateral surfaces of the condyles, on the contrary, constantly exhibit cartilage cells with offshoots of the first order, which are more numerous the farther away from the border of the articular surfaces. In the region where the basis-substance of the cartilage begins to be striated, we find the most beautiful silver images; here the coarse offshoots, interconnected by delicate ones, are very numerous, and remain so in the fibrous cartilage proper, and also in the tissue of the periosteum and the tendon, adjoining the hyaline cartilage.

My next purpose was to stain cartilage with chloride of gold. I placed the condyles of the knee-joint — the stump of the femur

FIG. 76.—HYALINE CARTILAGE FROM THE CONDYLE OF THE FEMUR OF AN OLD DOG, STAINED WITH CHLORIDE OF GOLD. [PUBLISHED IN 1872.]

C, dark violet cartilage corpuscles, with indistinct nuclei and numerous delicate dark violet offshoots. *B*, pale violet basis-substance, traversed by a partly dark violet, partly light, reticulum. Magnified 800 diameters.

again serving as a handle—into a one-half per cent. solution of chloride of gold, and traced its action on the cartilage for from ten minutes to twelve hours, always after rejecting the most superficial sections.

The gold stain of the cartilage corpuscles appeared in fifteen minutes; in the violet cell-body the nucleus became easily seen and sharply marked; the contour of the cell-body was also rendered more distinct. In many places the conical spokes

arising from the cell-bodies became violet, but could not be traced into the basis-substance any farther than in uncolored specimens; in specimens from the lateral surfaces, numerous coarse and thorny offshoots of a violet color were seen, similar to that of the cell-bodies themselves, while the basis-substance remained uncolored or was pale bluish-red.

After one hour's action of the gold solution, the coarse offshoots and the cells appeared dark violet, the offshoots of the second order became distinctly visible; some of the offshoots of the third order could be traced far into the basis-substance, or directly into cells near each other.

After twelve hours' action of the gold-solution, formations were brought into view which, being granular and crumbly, did not deserve attention. The cartilage cells were dark violet, the nucleus recognizable, if at all, as a lighter field. From all around the cell-body projected delicate offshoots, most of which looked finely granular, and in many places joined a granular reticulum. The reticulum is most abundant in the immediate vicinity of the cell and on the borders of the cell territories; it connects directly with neighboring cells, and in some places is so complicated that a precise definition is impossible, even with an immersion lens No. 10. In places where the image is incomplete, we can satisfy ourselves that we have to deal with a reticulum which is richly supplied with granular and varicose nodulations, and the connection of which with the cell-bodies is beyond doubt. Fig. 76 illustrates such a picture.

At the points of transition of cartilage into bone, there exists, as is well known, a layer of cartilage cells, the basis-substance of which is calcified. A calcareous deposition in the cartilage can be produced also by inflammation, following certain injuries of the cartilage. In horizontal sections of fresh, calcified specimens, as well as in specimens deprived of their lime-salts by chromic acid, we recognize that the basis-substance is traversed by channels, which hold offshoots emanating from the cell cavities, and producing a net work. The image of these offshoots is the same whether much or little lime-salt be present, either in the wall of the cavity bordering the cell-body or at the boundaries of the cell territories. We are satisfied that in all cases a deposition of lime-salts has taken place in the fields of the basis-substance, while the cell and its offshoots have remained unchanged. In old animals, where the calcified cartilage directly borders the bone-tissue, positive proof can be obtained that the "osteoid"

cells are, by means of offshoots, directly connected with the bone-cells.

The results of my researches lead to the following conclusions:

The bodies of the cartilage cells have radiating offshoots. These offshoots form a delicate varicose reticulum in the basis-substance. At the points of transition of hyaline cartilage into striated, fibrous cartilage and into periosteum, the offshoots are very large and broad; they connect neighboring cells, either directly or indirectly, by means of delicate offshoots.

In 1872 I was not yet acquainted with the structure of bioplasson—*i. e.*, the cell-body, nor had I then recognized the

FIG. 77.—HYALINE CARTILAGE IN TRANSITION TO STRIATED CARTILAGE, FROM THE BORDER OF THE CONDYLE OF FEMUR OF A GROWN DOG. STAINED WITH CHLORIDE OF GOLD.

C, dark violet cartilage corpuscles with distinct nuclei, projecting offshoots, *O*, which directly or indirectly connect the corpuscles, *B*, pale violet basis-substance, exhibiting a partly dark violet, partly light, reticulum. Magnified 800 diameters.

significance of the interconnection of cartilage corpuscles for elucidating biological views in every respect contradictory of the cell theory. Still, I felt confident that, on account of the sim-

plicity of the methods used, other investigators would encounter no difficulty in producing what I had produced and seeing what I had seen. But what happened was just the contrary. A large bulk of literature was produced on this subject; nevertheless, almost all observers failed in bringing to view the connections existing between the cartilage corpuscles. Some claimed that it was the synovial liquid which assumed, on treatment with nitrate of silver, the figures I described; others that the connections between the cartilage cavities could be found only in the superficial portions of the condyles; still others believed the formations seen by me to be artificial products, due to a precipitation of the metal-salt I had employed. All, however, agreed that the light reticula which eventually became visible in the silver-stained specimen were only juice-canals, according to views taken by Von Recklinghausen.

Meanwhile I had convinced many hundred students, in my laboratory in New York, that the cartilage corpuscles are really connected with each other, and an unprejudiced observer, L. Elsberg (see page 138), publicly announced his conviction of the correctness of my assertions.

In the first place, there could be no doubt that the negative image produced by the silver in every respect answers to the positive image brought out by the gold. The negative silver image obtained from the border of the condyles, where the hyaline cartilage begins to change into fibrous cartilage (see Fig. 75), fully corresponds with the positive gold image produced in the same place. Fig. 77 is an illustration of specimens which for years I have used for demonstrations in my laboratory.

Secondly, I was desirous of satisfying myself if the method of treatment with silver was really so unreliable as claimed by some writers. I gave Dr. W. Hassloch, a physician of unusual cleverness, attending my laboratory in 1878, my printed pamphlet containing directions for procedure, and the fresh condyles of a human fœtus, six months old. A few days later, without any further advice on my part, the gentleman showed me a large number of specimens, exhibiting images precisely similar to those illustrated in Fig. 78. The identity of the light spaces with cartilage corpuscles was beautifully demonstrated in the thin sections, where dark brown layers were directly followed by slightly stained or unstained layers.

I admit, however, that my assertions would not have deserved much attention had the staining methods with nitrate of silver

and chloride of gold been the only foundation on which they were based. But I said, in 1872, that calcified portions of the hyaline cartilage, the calcification being a product either of a normal process preceding ossification, or of a process of inflammation artificially induced, exhibited the reticulum and the offshoots of the cartilage corpuscles in the larger projections of the cavities, without the application of any re-agent. The increased refracting power of the calcified basis-substance is sufficient by itself to bring to view everything that can be seen in the silver and gold specimens, and everything which can be deduced from a comparison of both. The images obtained in the earliest stages of inflammation of any variety of connective tissue are very valuable means of convincing ourselves of the

FIG. 78.—HYALINE CARTILAGE FROM THE CONDYLE OF THE FEMUR OF A HUMAN FŒTUS, SIX MONTHS OLD. STAINED WITH NITRATE OF SILVER.

S^1, single light space; S^2, twins, directly connected by light lines; *B*, dark brown basis-substance pervaded by a light reticulum. Magnified 1000 diameters.

presence of a large amount of living matter within the basis-substance. There is, indeed, no way to understand the inflammatory process unless explained in this manner.

A. Spina (see page 141), by the alcohol treatment of the cartilage, discovered an excellent method for demonstrating the connections of the cartilage corpuscles. An eye with very little experience can observe to-day what, in 1872, I first maintained, after a long and tedious research and laborious experiments.

The Structure of the Thyroid Cartilage. By L. Elsberg.*

Longitudinal sections through the lateral plates of the thyroid cartilage of a man of about twenty-five years, hardened in chromic acid and stained with an ammoniacal carmine solution, exhibit with low powers of the microscope

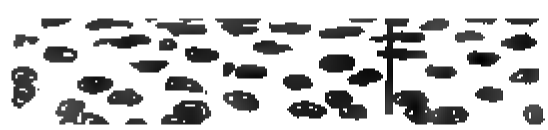


Fig. 79.—Plate of the Thyroid Cartilage of Adult. Longitudinal Section.

A, perichondrium toward the mucous membrane; *B*, perichondrium toward the skin; *F*, fibrous portion of cartilage in the center; *H*, hyaline portion, on either side, near the perichondrium. Magnified 150 diameters.

(150 to 200 diameters) the following: The cartilage corpuscles, either single, in pairs, or in groups of from three to six, or even more, are imbedded in a basis-substance which, for the most part, is homogeneous-looking or indis-

* "Contributions to the Normal and Pathological Histology of the Cartilages of the Larynx," Archives of Laryngology, vol. ii., 1881.

tinctly granular, but in some portions finely striated. The homogeneous or indistinctly granular-looking basis-substance is that which bears the name hyaline basis-substance; the striated is termed fibrous, although actual fibrillæ appear only on the edges of the specimen, or when the tissue is torn and mutilated. The fibrous basis-substance is intermixed, without any regularity, with the hyaline, and usually sharply separated from it. Not infrequently a number of cartilage corpuscles, or groups of cartilage corpuscles, are surrounded by fibrous basis-substance, the striations of which run, as a rule, in a sagittal direction, *i. e.*, vertical to the surface. Within the fibrous basis-substance the cartilage corpuscles are at most points sparsely scattered or absent; here and there, however, they are more numerous, in rows or elongated, corresponding to the direction of the striations. It also occurs that striated portions of the basis-substance contain very minute globular or oblong corpuscles, sometimes to such an extent that the striated structure is concealed by the large number of these corpuscles. (See Fig. 79.)

The fibrous portion is seen to occupy the center of a longitudinal section of one of the plates of the thyroid cartilage. This is not regularly the case in every cut, and was exceptionally well marked in the section from which the drawing was made. In some sections the fibrous cartilage is altogether absent, but every laryngeal cartilage contains some fibrous mixed with hyaline portions.

Under higher magnifying powers (500 to 600 diameters), single cartilage corpuscles exhibit features, frequently before described, with coarsely granular nuclei. Around the nucleus finer granules are visible. At the periphery of the cartilage corpuscle there are several strata of higher refracting power, especially the zone nearest the basis-substance, which, as a rule, appears very shining and is what is termed the capsule of the cartilage corpuscle. Not infrequently the cartilage corpuscle is very indistinct, being but slightly more granular than the surrounding basis-substance; then almost nothing but the nucleus marks its presence and its place. In twin formations of cartilage corpuscles, which are often met with, the zone of division between the two corpuscles is identical with that surrounding both, in the shape of a capsule. Of the same nature are the zones of division that are seen in clusters of cartilage corpuscles.

The so-called hyaline basis-substance throughout its whole extent now appears finely granular; as a rule, the granulation is more distinct midway between the corpuscles than in their immediate vicinity. The fibrous portions of the basis-substance are seen to be made up of extremely minute spindles, which, by being grouped longitudinally, produce the aspect of striation. The spindles or fibers are separated from each other by light rims, and both the spindles and the rims look finely granular. Between the spindles may often be seen small globular bodies, sometimes scattered, sometimes in clusters, of which the size and shape greatly vary, reaching occasionally the size and shape of a regular cartilage corpuscle. In some striated fields, blood-vessels, both arterial and capillary, can be seen; the former with the characteristic muscle-coat, the latter with the endothelial wall, besides holding red blood-corpuscles in their calibers.*

The highest powers of the microscope (1000 to 1200 diameters) reveal

* These striated fields are remnants of former medullary spaces, for the striated portions in the center of the cartilage never contain blood-vessels.

the reticular structure of cartilage corpuscles, as it is known since 1873. All granules within the nucleus and all granules within the corpuscle are uninterruptedly connected by delicate threads. The intranuclear net-work is connected with the corpuscular reticulum by radiating conical spokes traversing the light rim around the nucleus; and, at the periphery of the corpuscle, similar conical spokes pierce a narrow light rim and enter the basis-substance, in which, especially in the highly refracting zone termed capsule, they are usually lost to sight. Cartilage corpuscles, even, which have become so pale as to leave only a dim trace of their former contour visible, still exhibit more or less distinct traces of the reticular structure.

The same structure may be seen throughout the so-called hyaline basis-substance—more distinct in the middle of the space between the corpuscles than immediately around the corpuscles themselves. The fibrous portion of

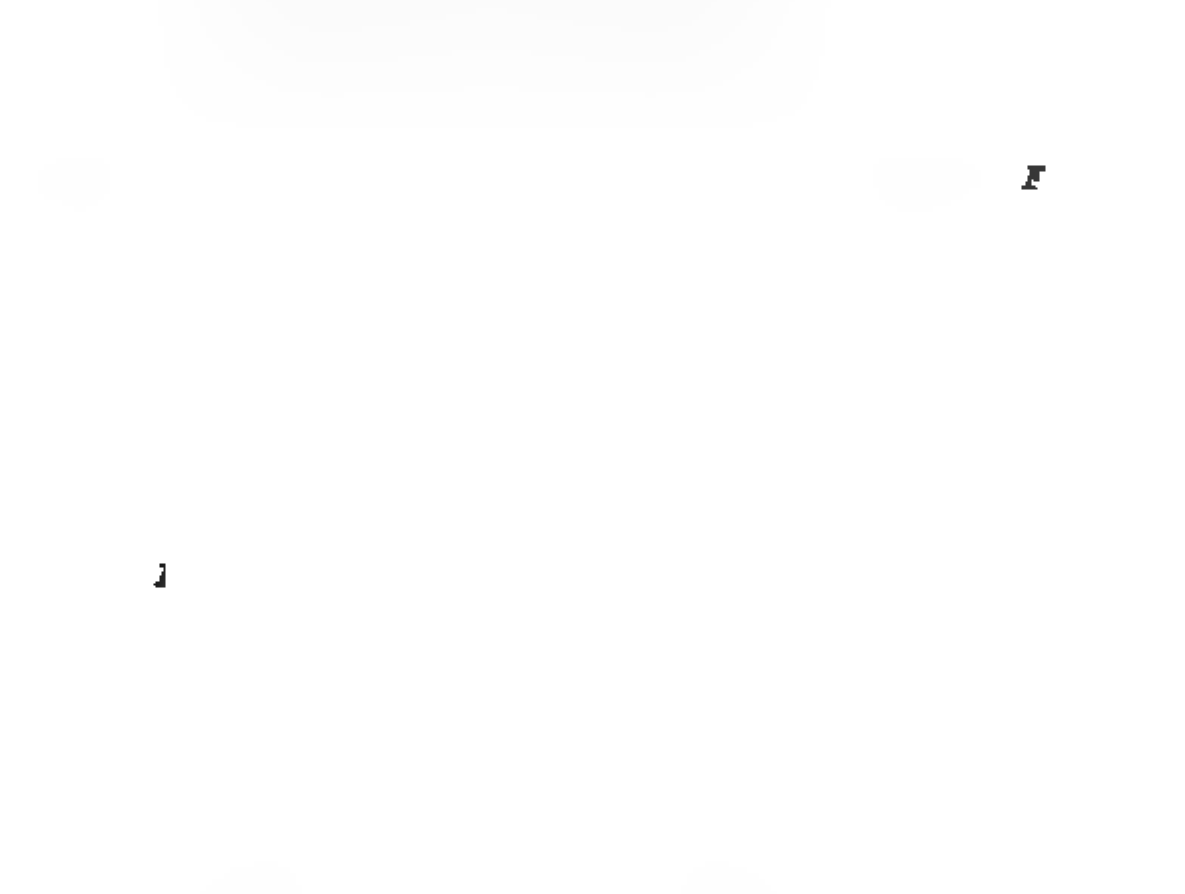


Fig. 80.—Thyroid Cartilage of Adult. Sagittal Section.

C, C, cartilage corpuscles; *B*, indistinctly reticular hyaline basis-substance, *F*, fibrous basis-substance. Magnified 1200 diameters.

the basis-substance has also a reticular structure. The bodies of the slender spindles show a net-work without the application of any re-agent, and the light rims between the spindles are traversed by delicate threads running in a vertical direction to the longitudinal diameter of the spindles. All granules and lumps scattered through the fibrous basis-substance are surrounded by light rims, which are pierced by conical spokes inosculating with the reticulum of the neighboring spindles. (See Fig. 80.)

I have treated sections of the same cartilage, after they had for several days been washed out with distilled water, with a one-half per cent. solution

of gold chloride, whereupon they assumed a dark purple color, and showed all the features described, somewhat more distinctly than simple carmine preparations. I deem their detailed description unnecessary.

When I became acquainted with Spina's researches (see page 141), I deemed it of importance to repeat the examination according to his method. I therefore placed a larynx, immediately after removal from the body of a girl, aged twenty-four years, into strong alcohol, and after four days made thin sections from the thyroid cartilage in a horizontal direction, transferred them in alcohol to the slide, and examined them with both low and high powers, adding, from time to time, a drop of strong alcohol to prevent the specimen from drying. The appearance presented by such a specimen is truly surprising. As a matter of course, the cartilage corpuscles are shriveled up, so that more or less space is left between their jagged periphery and the bor-

F[illegible] [illegible]G
ALCOHOL. HORIZONTAL SECTION.

C, shriveled cartilage corpuscle; *O*, longitudinal offshoots; *R*, reticulum in basis-substance; *G*, granules of living matter. Magnified 1200 diameters.

der of the basis-substance. With an amplification of 500 diameters, the basis-substance is seen pierced by light filaments, which, in many instances, can be traced through the intervening space into the body of the cartilage corpuscle. Most of these filaments radiate around the corpuscle, and, immediately after penetrating the basis-substance, diverge and form a reticulum throughout its extent. Cartilage corpuscles located near each other are directly connected by non-ramifying, and occasionally by ramifying, offshoots, or by bundles of such offshoots of a more or less parallel course. The reticulum in the basis-substance is either radiating or irregularly arranged around

the corpuscle. Contrary to the assertion of Spina, the filaments or offshoots do, as a rule, ramify, except those that directly connect the neighboring corpuscles. Sometimes thick bundles of offshoots emanate from opposite poles of the corpuscles, while intervening portions of the periphery are almost devoid of offshoots. Toward the periphery of the thyroid cartilage,—where, as is well known, the cartilage corpuscles elongate, becoming smaller and spindle-shaped and more or less parallel to each other,—the offshoots are given off rectangularly to the axis of the corpuscles.

High magnifying powers, immersion lenses No. 10 and No. 12, conclusively prove the connection of the offshoots with the cartilage corpuscles. Portions of the basis-substance which, with lower powers, looked only granular, now show a delicate reticulum, which, even when coarser offshoots are

FIG. 82.—THYROID CARTILAGE OF ADULT. HORIZONTAL SECTION.

C, C, cartilage corpuscles; *F*, fibrous portion of cartilage; *G*, granules of living matter. Magnified 600 diameters.

wanting, is connected with the cartilage corpuscle through delicate and more or less conical offshoots from the surface of the corpuscle.

The light interstices between the fibers of striated basis-substance are also traversed by delicate grayish thorns. Such thorns are visible even in the perichondrium. Through the fibrous bundles of the perichondrium run, in a nearly rectangular direction, delicate light streaks, while the interstices between the bundles, and the spaces left between the corpuscular elements and the bundles, exhibit delicate conical grayish threads, the direction of which corresponds to these light streaks. (See Fig. 81.)

The highest powers of the microscope disclosed in one of the specimens examined another feature in the hyaline basis-substance, viz.: the presence of a number of granules or minute lumps of varying shape, some interwoven

with the direct offshoots of the corpuscles, and some with the threads forming the finer net-work of the basis-substance. They appeared to be thickened points of intersection, knots, or nodes, composed of the same material as the offshoots and threads themselves. They were unquestionably granules of living matter. I found their greatest development in a case examined without Spina's method—a case which I shall describe presently.

The observation which I am now about to record was made in specimens of the thyroid cartilage removed from the body of a rather stout man, forty-eight years old. After having been hardened in chromic acid solution, without any other re-agent, they exhibited formations in the basis-substance which, so far as I am aware, have never before been described. I have alluded to them as

FIG. 83.—THYROID CARTILAGE OF ADULT. HORIZONTAL SECTION.

C, cartilage corpuscle; *B*, hyaline basis-substance; *G*, granules of living matter. Magnified 1200 diameters.

found in one of the specimens examined, with the highest powers of the microscope, by the alcohol method of Spina.

As to the cartilage corpuscles in these specimens, many of them were larger and more coarsely granular than are commonly observed; otherwise, their characters and the arrangements of the basis-substance, both so-called hyaline and fibrous, were like those described before. The intranuclear, intracorpuscular, and intercorpuscular net-works were with high powers well shown.

The very remarkable feature was that, with quite low power, the basis-substance was seen to be speckled and studded with granules or lumps, varying from that of a point at the limit of the visible to that approaching the dimen-

sions of a regular cartilage corpuscle. Of course, no one must for a moment think of anything like the pathological conditions that have been described, either as granular degenerations of the cartilage basis-substance, or as incrustations of the corpuscles. Not only were the appearances entirely different and the cartilage healthy,—as otherwise ascertainable, as well as from the known condition of the man and of the cause of his death,—but the true nature of the lumps was made perfectly clear by examination with higher powers. (See Fig. 82.)

When magnified to the extent of 600 diameters, the same relative appearance was preserved. The lumps in the basis-substance still varied in size, from the limit of the visible to the magnitude of ordinary cartilage corpuscles; but, in all the larger lumps, differentiations were visible which approached them in structure, as well as in size, to cartilage corpuscles. In some, one or more vacuoles, in others, a small or large nucleus, or even two nuclei, could be made out; and a few (*i. e.*, occasionally one in some fields) showed irregular twin, or even triplet, formation.

The highest power threw a wonderful light upon these lumps. They were seen to be masses of living matter. The larger showed a net-work in their interior, some without and some with a nucleus, and the latter, when present, was sometimes homogeneous and sometimes reticulated. All the lumps, except the smaller, were surrounded by a distinct light seam, through which radiating conical offshoots passed to the net-work in the basis-substance; and all of them, even the smallest, sent delicate offshoots connecting them with that net-work, or were themselves part and parcel (*i. e.*, thickened points of intersection of the threads) of that net-work. (See Fig. 83.)

After having studied such a specimen, it was easy to interpret correctly the intrareticular granules seen in the alcohol specimen represented in Fig. 81.

*Development of Cartilage.** Hyaline cartilage is developed, in the same way as fibrous tissue and bone, from the indifferent medullary elements which, in human embryos, between the fourth and fifth month, and in newly born dogs, cats, and rabbits, are stored up in a still considerable amount in the vascularized medullary spaces of the cartilage.

Upon the authority of Schwann, the erroneous view has been generally held that blood-vessels are found in hyaline cartilage only a short time before commencing ossification. In early periods of development of cartilage, medullary spaces are present containing blood-vessels,—viz.: arteries, veins, and capillaries,—which, as Bubnoff † has demonstrated, are preserved to quite an advanced age.

In such spaces we find, besides a varying number of blood-

* "Untersuchungen über das Protoplasma. IV. Die Entwickelung der Beinhaut, des Knochens und des Knorpels." Sitzungsber. der Akad. d. Wissensch. in Wien, 1873.

† Sitzungsber. der Wiener Akademie d. Wissensch., 1868.

vessels, medullary tissue, consisting of globular or spindle-shaped corpuscles, with a slight amount of a myxomatous and fibrous reticular basis-substance. Lower powers of the microscope reveal that the boundary line between medullary and cartilage tissue in some places is sharply defined, while in other places it is indistinct or invisible. In the most peripheral portions of the medullary tissue, *i. e.*, nearest the cartilage, we see rows of spindle-shaped or oblong bodies, bearing a close resemblance to the medullary corpuscles found on the boundaries of forming bone-tissue. (See Fig. 84.)

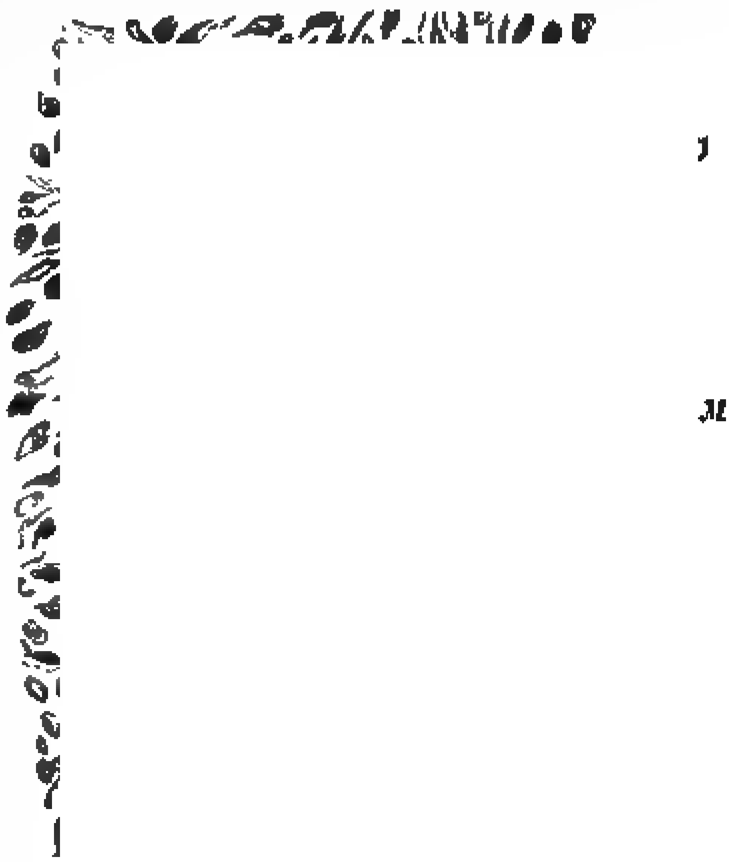


FIG. 84.—HYALINE CARTILAGE OF THE CONDYLE OF TIBIA OF A HUMAN EMBRYO, FOUR MONTHS OLD. SAGITTAL SECTION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

M, medullary canal, transversely cut, containing blood-vessels and medullary tissue; *C*, cartilage, with marked territories in the basis-substance. Magnified 200 diameters.

In the cartilage of the knee-joint, at the extremity of the femur of new-born pups, we meet not infrequently, at the borders of a medullary space, close to the fully formed cartilage, with groups of medullary corpuscles, the peripheral portions of which are beginning to be infiltrated with an apparently homogeneous basis-substance, while the central portion retains the character of the cartilage corpuscle. Under these conditions, homogeneous (in the optical diameter semicircular) fields are projected into the caliber of the medullary space. Or a gradual transition of medullary into cartilage tissue takes place at the border of the medullary space, with the result that a number of spindle-shaped medullary corpuscles are transformed into a territory of cartilage tissue, which in this situation sometimes exhibits a delicate

striation. In the first case, the result is a globular territory with a central cartilage corpuscle; in the latter, a spindle-shaped territory, containing an elongated, spindle-shaped corpuscle. (See Fig. 85.)

There is a marked difference, however, between the territories of the cartilage in very young and in fully developed animals. In the articular cartilage of human embryos from four to five

V

I

B¹

B²

FIG. 85.—HYALINE CARTILAGE OF THE CONDYLE OF FEMUR OF A NEW-BORN PUP. SAGITTAL SECTION. CHROMIC ACID SPECIMEN, SLIGHTLY STAINED WITH CHLORIDE OF GOLD. [PUBLISHED IN 1873.]

V, loop of a capillary blood-vessel in a medullary canal of the cartilage; *I*, elongated medullary corpuscles in the stage of indifference, *B¹*, boundary zone of basis-substance. *B²*, fully developed basis-substance. Magnified 800 diameters.

months old, and that of newly born dogs and cats, the latter being at birth as far advanced in development as man at four or five months, we see territories only, with numerous cartilage corpuscles, between which the basis-substance is scanty, as if sprung

from a few embryonal (medullary) corpuscles, or from a single corpuscle. In the full-grown animal, on the contrary, the territory contains but one or a few cartilage corpuscles, the double and triple formations, between which the basis-substance is very scanty or even absent, while in the peripheral portion of the territory a large amount of basis-substance is found, which must have originated from a corresponding large number of embryonal (medullary) corpuscles. Although the cartilage corpuscles of very young animals are decidedly smaller than those of the full-grown, there is not the slightest evidence of a so-called "interstitial growth," *i. e.*, an increase of the bulk of the corpuscle as well as of the basis-substance already formed. It is far more probable that the embryonal cartilage is not the same formation from which the cartilage of the adult arises; it certainly is not in the same location as far as the size of the whole body is concerned. Besides, a fully formed cartilage, or any other tissue, grows, during the time that the cartilage is returning to the medullary condition, only in limited places, when a new grouping of medullary corpuscles takes place, and a new basis-substance is developed.

Those who maintain that an "interstitial" growth takes place, forget that a cartilage corpuscle, once imbedded in the dense, chondrogenous basis-substance, cannot increase in size unless a liquefaction of the basis-substance has occurred, at least at the borders of the cavity containing the corpuscle. The same objection can be raised against the hypothesis of the division of cartilage corpuscles in the fully developed tissue. The probability is far greater that cartilage grows with the growth of the whole body, from medullary corpuscles at the periphery, while the central portions are reduced into medullary tissue for the benefit of the growing bone-tissue. The "apposition theory" considered in this light is the only legitimate one, as there is no difficulty in understanding that from the perichondrium, or other peripheral formations of connective tissue, always, of course, through the intervening stage of medullary tissue, new cartilage is produced during the whole period of development of the body.

The process of development of cartilage with striated basis-substance is materially the same as that of hyaline cartilage, as I could trace on the lateral surfaces of the condyle of femur of growing rabbits. Here we find intermediate striated cartilage between the hyaline cartilage and the tendon or ligamentous tissue; and the intermediate striated portions may be found to contain fields of hyaline cartilage. With such evidences it is not

difficult to convince oneself that the character of the cartilaginous basis-substance, whether hyaline, striated, or fibrous, depends upon the shape and the grouping of the original, indifferent medullary corpuscles alone.

The cartilaginous callus, obtained after subcutaneous fractures of the leg-bones of dogs and cats, I found very suitable for the study of the development of cartilage. Here the new formation of cartilage arises from nests, identical with medullary spaces, which in their center contain blood-vessels, at their periphery spindle-shaped elements, as the result of the inflammatory new formation. The medullary elements close around the blood-vessel are globular, and are succeeded by layers of spindle-shaped bodies, the nuclei of which are partly faded, indicating that these formations are in the stage of transition from a uniform granulation into the stage of infiltration with glue-yielding basis-substance. In such inflammatory nests, also, we observe the transformation of capillary blood-vessels into solid strings, and afterward into small medullary elements. The process is the same as in the involution of bone-tissue, due to normal senile changes. In the same cartilaginous callus we also encounter numerous nests in which red blood-corpuscles and blood-vessels arise from cartilage corpuscles (see page 98), and these formations precede the liquefaction of the calcified cartilaginous basis-substance, which occurs previously to the production of new medullary tissue and of bone.

The embryonal or medullary elements are, under all circumstances, the formers of tissue. Those from which bone arises have been termed "osteoblasts" by Gegenbaur, who considered them to be, specifically and exclusively, bone-formers. We are far from understanding the specific nature and limits of embryonal corpuscles, and the designation "osteoblasts" is therefore superfluous. We might with equal propriety speak of "periostoblasts," "chondroblasts," etc., while, in fact, all these tissues originate from one and the same source—namely, the *medullary tissue.* What character the territory will assume, what will be the nature of the basis-substance in the territory, depends upon the grouping of these many-named "blasts" in the stage of indifference preceding the new formation of a tissue.

In 1873, I admitted the possibility that, under certain physiological conditions and changes, one variety of basis-substance might be directly transformed into another; periosteum, f. i., into bone or into cartilage, hyaline into striated cartilage, etc. This

possibility seems to me, to-day, to be very slight, so much so that even a direct transformation of hyaline into fibrous cartilage is doubtful. *I am positive that one variety of basis-substance, one kind of connective tissue, can never be transformed into another except through the intermediate stage of medullary tissue. A completely developed tissue must first return to the embryonal condition, before a new and different tissue can develop from it.*

Remak * was the first to approach our present views respecting the formation of basis-substance of cartilage. He maintained that it is deposited between the outer and the inner membrane of the cartilage-cell, whereupon the outer membrane perishes, and the shells of the "parietal substance" fuse together in order to form the intercellular substance.

E. Brücke, † in accordance with the views held by Max Schultze, considered the outermost layer of the cartilage cells, destitute of a membrane, to be the former of basis-substance proper. The layer close around the unchanged portion of the cell-body he asserts to be more dense than the rest of the basis-substance, and this condensation causes the appearance of a capsule. Similar views are held by R. Heidenhain ‡ concerning the formation of single and stratified capsules. If these views were correct in every respect, we ought to find in developing cartilage enormous corpuscles, corresponding in size with the whole territory, before the changes at their periphery had ensued. But the facts are just the contrary to this, for in the embryonal cartilage the corpuscles are decidedly smaller than in that of the adult.

A. Spina § demonstrates that, in fully developed cartilage, with advancing age the amount of basis-substance increases at the expense of the cartilage corpuscles. These become pale, finely granular, destitute of nuclei, and then disappear in the basis-substance. The protoplasmic reticulum of the cells, he says, does not perish, but remains, somewhat altered in its character, in the basis-substance. This explains why, in the articular cartilage of the very aged, the corpuscles are so extremely scanty and small.

* Müller's Archiv, 1852.

† "Die Elementarorganismen." Sitzungsber. d. Wiener Akademie d. Wissensch., 1861.

‡ Studien des Physiol. Instit. zu Breslau, 1863.

§ "Untersuchungen über die Bildung der Knorpelgrundsubstanz." Sitzungsber. d. Wiener Akademie d. Wissensch., 1880.

I can fully corroborate Spina's assertions from my own observations.

(4) Bone Tissue.

History. The growth of the bones was the subject of careful studies in the seventeenth and eighteenth centuries, long before anything positive was known as to their structure. Adrianus Spigelius * was the first to maintain that the bones grow either from cartilage or by apposition.

Clopton Havers † found that bone arises from cartilage.

Robert Nesbitt ‡ says that "there is not one single phenomenon to support the notion of bones being nothing but indurated cartilage, or that they are produced only by a transmutation of a cartilaginous substance, and al[illegible] bony productions are caused entirely by the apposition of cretaceous matter."

In the middle of the eighteenth century, Duhamel, § after experiments by systematically feeding various animals with madder, asserted that the bones grow from the periosteum, and was contradicted by A. Von Haller, who denied any participation of the periosteum in the process. Exactly the same fight is carried on even in our day.

John Hunter ‖ found in the growth of bones "two processes going on at the same time, and assisting each other: the arteries bring the supplies to the bone for its increase; the absorbents at the same time are employed in removing portions of the old bones, so as to give to the new the proper form. By these means the bone becomes larger, without having any material change produced in its external shape."

J. Howship ¶ speaks of lining-membranes of the canals of the bone carrying the blood-vessels; he did not see the lining in full-grown bone, "possibly because the circulation of the red blood is more limited in full-grown than in young bone." He gives illustrations of lacunar widenings of the canals, evidently caused by a morbid process.

After the bone-corpuscles (lacunæ) and their canaliculi were made known by Purkinje and Deutsch (1834), Johannes Müller [1] pointed out their connection, and suggested that all these spaces are filled with lime, and should, therefore, be termed canaliculi chalicophori.

Lessing [2] first drew attention to the fact that the dark appearance of the lacunæ and canaliculi, seen in specimens from dry bone, is due to their containing air, and was inclined to regard them as a lacunar system, filled, in living bones, with fluid. Klebs, much later, made the wonderful discovery that the contents of these spaces in older, even fresh bones, are of a gaseous nature.

* "De Formatione Fœtu," 1631. The early literature is found in Alb. Kölliker: "Die Normale Resorption des Knochengewebes." Leipzig, 1873. The later literature, from 1836 to 1878, is given by M. Kassowitz: "Die Normale Ossification," etc. Wiener Med. Jahrbücher, 1879.

† "Osteologia Nova; or, Some New Observations in the Bones." London, 1691.

‡ Human Osteogeny, explained in two lectures. London, 1731.

§ "Mémoires de l'Académie de Paris." 1742.

‖ "Experiments and Observations on the Growth of Bone," from the papers of the late Mr. Hunter, by Everard Home. London, 1798.

¶ "Microscopic Observations on the Structure of Bone." Medico-Chirurgical Transactions. London, 1816.

[1] Müller's Archiv, 1836.

[2] "Ueber ein plasmatisches Gefäss-System in allen Geweben, insbesonders in Knochen und Zähnen." Hamburg, 1846.

R. Virchow * claimed that the lacunar and canalicular spaces are really plasmatic, and can be isolated, as true "bone-cells," by the treatment of dry bone with acids. He was contradicted by E. Neumann, † who conclusively proved that Virchow's branching cells are nothing but the densified walls of the lacunæ and the larger canaliculi resisting the action of strong acids and alkalies (elastic substance). Such a substance was found to line also the Haversian canals.

A. Kölliker ‡ declared that on the external surfaces of growing bones an absorption takes place. Virchow, in 1853, § agreed that such an absorption occurs on the cerebral surfaces of the skull-bones. Virchow had, in 1852, asserted that the bay-like excavations (so-called Howship's lacunæ) on the surface of pathological bones are due to a melting of the substance of the bone, in correspondence with the cell territories; afterward, he maintained that the bone-cells set free by the solution of the intercellular substance, are transformed into medullary cells.

Tomes and De Morgan ‖ observed erosions in carious and provisional teeth, and argued in the following manner: "When we connect this condition with the fact that the nucleated cells, which form the embryo, have the power of appropriating the material which lies about them to the purpose of their own growth, . . . it is difficult to resist the belief that the cells which lie in contact with wasting bone and dentine take up those tissues. . . . An objection may be raised to the supposition that the bone is absorbed by cells, on the ground of the density of the former; but it must be borne in mind that, as the density is gradually imparted to the bone through the agency of the adjoining soft parts, there seems no good reason for disbelieving that they may also be instrumental in its removal." ¶

Heinrich Müller, in 1858,[1] published his epoch-making researches on development of bone, which are the foundation of our modern views on this subject. His observations will be dwelt upon in the article on development of bone. Reference will there also be made to the researches of Gegenbaur (1865) and Waldeyer (1865).

Ed. Láng[2] was the first to ascertain that, in bone-specimens of recently killed animals, the lacunæ contain protoplasm, which is, to a certain degree, endowed with the property of amœboid motion, and from which starts the inflammatory new formation.

In the last decennium, a lively controversy was carried on regarding the question whether or not a growth of the bone by expansion, a so-called interstitial growth, occurs.

Ruge,[3] as the result of his counting and measuring the distances between bone-corpuscles, became a defender of the theory of interstitial growth. Jul. Wolff[4] energetically maintained an interstitial growth, and denied any appo-

* "Würzburger Verhandlungen," 1850.

† "Beiträge zur Kenntniss des norm. Zahnbein- und Knochengewebes." Königsberg, 1863.

‡ "Mikroskopische Anatomie," 1850.

§ Virchow's Archiv, Bd. iv. 1852; Bd. v. 1853.

‖ "Observations on the Structure and Development of Bone," 1852. Philosophical Transactions, 1853.

¶ All quotations from authors in this historical sketch are from Kölliker *(l. c.)*.

[1] "Zeitschrift für Wissensch.-Zoologie." Bd. ix.

[2] "Untersuchungen über die ersten Stadien der Knochenentzündung." Wiener Mediz. Jahrb., 1871.

[3] Virchow's Archiv. Bd. 49.

[4] Virchow's Archiv. Bd. 50.

sition from cartilage and periosteum. Lieberkühn,[*] on the contrary, fully corroborated the old and well-established views of an apposition. Recently, again, Strelzoff[†] favored the view of an interstitial growth, and was contradicted by Steudener,[‡] who demonstrated that the bone-corpuscles with advancing age decrease somewhat in size, and consequently appear to become farther apart as the bulk of the basis-substance increases.

V. Ebner[§] has arrived at the conclusion, based on macerations of bone in a ten to fifteen per cent. solution of chloride of sodium, to which he added one to three per cent. muriatic acid, that the lamellæ of bone-tissue are composed of fibrillæ. These fibers, according to him, can be isolated only for short distances, as they are interwoven and held together by a cement-substance containing the lime-salts, while the fibrillæ themselves are glue-yielding, but destitute of lime-salts. Fibers running from a lamella to the surface of the bone constitute the perforating fibers of Sharpey.

C. Langer[‖] added valuable contributions to the knowledge of the distribution of blood-vessels in shaft and flat bones.

M. Kassowitz[¶] published an extensive article on the formation of bone with special reference to the periosteal cartilage.

Methods. It is one of the strangest facts in histology that, although for a number of years dry specimens of tissue have been acknowledged to be worthless for microscopical research, bone even in our day is studied in the dry condition. All books of all nations on histology give accurate directions for slicing dry bone and grinding the sections thin for mounting in Canada-balsam. Such specimens are of little value for examinations with the microscope. Specimens of dry bone are about as useful for obtaining histological facts as are the silver-stained specimens of other tissues—*i. e.*, both exhibit the frame of the tissue, while all the soft parts, the real seats of life, are destroyed.

There is but one way to render bone-tissue suitable for study, and that is by softening fresh bone in a one-half per cent. solution of chromic acid, to which from time to time very small quantities of dilute hydrochloric acid may be added. If the chromic acid solution be changed every fourth or fifth day, and if a large quantity of the liquid be used for small pieces of bone, in a few weeks the specimens can be easily cut with the razor. This method was introduced by H. Müller in 1858, but has been far too much

* Sitzungsb. d. Marburger Gesellsch., 1872.

† Untersuchungen aus dem Pathol. Inst. zu Zürich, 1873.

‡ "Beiträge zur Lehre von d. Knochenentwicklung." Abh. der Naturf. Ges. zu Halle, 1875.

§ "Ueber den feineren Bau der Knochensubstanz." Sitzungsber. d. Wiener Akad. d. Wissensch., 1875.

‖ "Ueber das Gefäss-System der Röhrenknochen." Denkschriften der Wiener Akademie d. Wissensch., 1875. "Ueber die Blutgefässe der Knochen des Schädeldaches." Denkschriften d. Wiener Akademie der Wissensch., 1877.

¶ "Die Normale Ossification," etc. Wiener Mediz. Jahrbücher, 1879.

neglected. The best specimens are obtained from portions in which the basis-substance is not entirely decalcified, as in these the bone-corpuscles and their offshoots, as well as the corresponding cavities in the basis-substance, the lacunæ and canaliculi, are best preserved. For mounting, only dilute glycerine should be used.

A number of examiners have attempted to settle the question whether the lime-salts are deposited mechanically in the basis-substance, or whether there is a chemical union of the molecules of lime and glue. The question probably will never be satisfactorily answered. This much is certain, that by the extraction of the lime-salts by means of chromic acid, no material changes are produced in the glue-yielding basis-substance.

Bone-corpuscles. As early as in 1850, R. Virchow discovered the identity of the "bone-cells" with other "connective-tissue cells." Though he at first held the mistaken idea that the walls of the cavities were the bone-cells proper, he admitted later that the cavities, being hollow and filled with a liquid, hold the bone-cells. He was the first who recognized them to be the seats of life, and able to proliferate and produce medullary tissue.

As late as 1871, Ed. Láng, in Stricker's laboratory, recognized the bone-corpuscles to be living matter or protoplasm in the fresh condition, endowed with the property of amœboid change. In this view the bone-tissue, as well as every other variety of connective tissue, is built up by a calcified, glue-yielding basis-substance, containing scattered cavities and outlets of the cavities—the lacunæ and canaliculi of former histologists; the lacunæ are filled with living matter, the bone-cells or bone-corpuscles. Nothing positive was known at that time as to the contents of the canaliculi.

In 1872,* I undertook to study bone-tissue, both in fresh and preserved specimens. In fresh sections, taken from the condyle of the femur of young rabbits, transferred to the slide together with a drop of a one-half per cent. solution of table-salt, or, still better, of Müller's liquid, with an immersion lens No. 10 of Hartnack, I recognized the bone-corpuscles. They were round or oblong bodies of a grayish tint, lying in a shining basis-substance, which appeared traversed by numerous light canals.

* "Studien am Knochen und Knorpel." Wiener Mediz. Jahrbücher, 1872.

In the bodies, which were indistinctly spotted, I could often see a nucleus-like formation, with scalloped outlines. "The cell-body," I said, "is surrounded by a light, narrow zone, in which numerous conical offshoots are visible, emanating from the cell-body, and exhibiting the same character as the cell-body." In many places I could trace these extremely delicate, branching offshoots for a considerable distance in the basis-substance, and I saw them unite with the offshoots of neighboring corpuscles. When the offshoots could not be followed far away from the body, I found their continuations to be the light, branching canals in the basis-substance.

The offshoots and their anastomoses I could see very plainly in specimens stained with chloride of gold, where the dark violet bone-corpuscles were seen sharply defined upon the pale violet basis. The offshoots were likewise distinctly visible in specimens of bone, decalcified by lactic acid. With this method the corpuscles seemed not to have shriveled, as the rim between them and the basis-substance was not broader than in fresh specimens.

In specimens preserved in chromic acid, the bone-corpuscles appeared somewhat shriveled. The basis-substance inclosing their cavity was traversed by numerous canals. Most of the offshoots of the corpuscle resembled conical thorns, which terminated in fine points toward the calibers of the canals, but only in a few of these could I discern a granular substance which possessed the characteristics of the corpuscle.

In normal bone, I was convinced that the bone-corpuscles had offshoots which partly projected in the canaliculi, partly inosculated with each other. A plain view of these offshoots, however, could be obtained only in bone, in which an inflammation had been artificially induced. One of the first noticeable changes in osteitis was the swelling of the corpuscle and the increased distinctness of its offshoots. These observations are illustrated on page 126, Fig. 40.

In 1872 I was not aware of the significance of the union of the bone-corpuscles, and it was not until a year later that I made use of the structure of bone-tissue for pointing out new biological views. I have been led, by careful researches of osteitis, to the conviction that the basis-substance must be pervaded by a large amount of living matter in reticular arrangement, which after liquefaction of the basis-substance is freed and participates largely in the inflammatory new formation. Direct proofs of the presence of

this extremely delicate reticulum I could not obtain, as all trials with silver and gold staining of bone proved to be failures.

The bone-corpuscles, as well as all other connective-tissue corpuscles, are formations of living matter, which in a juvenile condition are found to be compact, homogeneous, or vacuoled lumps, while in full development they are nucleated plastids. Their shape varies, to some extent, with that of the territories of basis-substance in which they exist. We find globular bone-corpuscles, which have assumed a star-shape by the appearance of numerous radiating offshoots, in the earliest formations of globular territories. We also meet with globular bone-corpuscles at the peripheral portions of fully developed Haversian systems, owing to the presence of the first formed territories of this system, and again in the interstitial bone-tissue between the systems, in places where no lamellæ are formed. In striated or lamellated bone-tissue the corpuscles are oblong or spindle-shaped bodies, slightly bent in the direction of the striæ or lamellæ, interconnected by larger offshoots, emanating from both poles, and by numerous delicate offshoots, traversing the basis-substance in a rectangular direction. The latter offshoots arise at right angles from both the periphery of the corpuscles and their larger longitudinal branches. In the Haversian systems the bone-corpuscles are slightly flattened, and in longitudinal sections exhibit their broadest oblong surface whenever the razor strikes a peripheral portion of a Haversian system, while they have the appearance of narrow spindles, when the razor runs through the middle of a lamellated system. In transverse sections of the system the corpuscles exhibit irregular shapes, and again vary in their diameters according to the depth to which they are cut by the razor. A spindle will necessarily look broader if the section has been made transversely through the middle, and narrow if near the ends.

Varieties of Bone-tissue. There are two kinds of bone-tissue, which, in the fully developed subject, however, are always combined with each other, viz.: the cancellous, epiphyseal, or spongy bone-tissue, and the compact or cortical bone-tissue.

(a) Cancellous, Epiphyseal, or Spongy Bone-tissue is built up by trabeculæ, arranged as a frame-work inclosing the medullary spaces. It is the only kind found in early stages of development of bone. In the fourth, fifth, and sixth months of embryonal life of human beings, and in dogs, cats, and rabbits at birth, no other bone-tissue but the cancellous is found. In

the juvenile skeleton, this structure composes the epiphyseal ends and the central portions of the shaft-bones, and the central portions of flat and short bones. (See Fig. 86.)

Cancellous bone-tissue of the embryo is invariably striated and non-lamellated. In the fully developed skeleton it exhibits usually indistinct lamellæ. The spaces between the trabeculæ of cancellous bone are in youth filled with a richly vascularized medullary tissue, the "red medulla" of Virchow; while with

FIG. 86.—TIBIA OF A NEWLY BORN PUP. LONGITUDINAL SECTION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

T, trabeculæ of bone-tissue containing bone corpuscles; *M*, medullary spaces filled with medullary tissue, holding blood-vessels in the most central portions. Magnified 200 diameters.

advancing age the spaces exhibit fat-tissue, Virchow's "yellow medulla."

In very old persons there is an increasing deficiency of both the cancellous and compact bone-tissues; the bone corpuscles are also very small and few in number, as many of them have been transformed into basis-substance.

The relation between the cancellous and the compact structure differs in different bones. As a rule, the short bones are largely

made up of cancellous tissue, with only a thin layer of compact bone at their peripheries. Flat bones exhibit the cancellous structure in the middle portion, the diploë of skull-bones, while the layers on the outer and inner surface are formed entirely of compact bone, the outer layer being generally broader and richer in blood-vessels than the inner. Thin, small, flat bones, such as the ethmoideal, turbinate, etc., may be considered as flattened trabeculæ of the cancellous variety. The shaft-bones have a broad investment of compact structure in their middle, *i. e.*, diaphyseal portion, while this tissue gradually decreases toward the ends, the epiphyses. These parts, as well as the large central marrow space, exhibit the cancellous structure in greatly varying amounts. H. Meyer first drew attention to the fact that the trabeculæ of the cancellous structure, especially in the epiphyseal extremities of shaft-bones, were built up according to a certain law, and J. Wolff, with the assistance of Culmann, has explained, according to mathematical principles, the regular arrangement of the trabeculæ in the directions of lines of pressure and traction.

(b) Cortical or Compact Bone-tissue is composed of parallel lamellæ, closely packed together in intimate relation with the blood-vessels. The cortex of both flat and shaft bones consists of a concentric system of lamellæ surrounding the central marrow space, and this concentric system in its middle portion is traversed, usually at right angles, by a number of systems of lamellæ, each surrounding a central blood-vessel. Thus, two peripheral systems of lamellæ originate, of which the outer is always the broader, and well marked, the inner often but little developed.

The middle portion, lying between the two peripheral systems, is traversed more or less rectangularly by the Haversian systems. In *transverse sections* of the cortex of shaft-bones, the lamellæ of the two peripheral systems run longitudinally, while the Haversian systems are cut transversely or obliquely. Between the latter there are the longitudinal lamellæ of the so-called "interstitial or intermediate" bone-tissue. (See Fig. 87.)

The Haversian system is composed of lamellæ which are disposed in concentric layers around capillary blood-vessels. Such systems of lamellæ are regularly arranged in the cortex of the long bones, and irregularly in the cortex of flat bones. The outer contour of a system is never smooth and even, but composed of a number of shallow protrusions, viz., the first-formed territories, and the aggregation of these formations gives the outer contour

of a Haversian system a fluted appearance. The systems are sometimes found close to each other, with very little intermediate bone-tissue between them; or they may be more or less apart, with a distinctly lamellated intermediate bone-tissue

FIG. 87.—FEMUR OF A GROWN CAT. CORTICAL PORTION, TRANSVERSE SECTION. BLOOD-VESSELS INJECTED.

R, the outer peripheral system of lamellæ; *R'*, the inner peripheral system of lamellæ; *H*, the intermediate system of lamellæ, traversed by smaller so-called Haversian systems cut in transverse and oblique directions. Magnified 50 diameters.

between them, the lamellæ of which run in a direction more or less parallel with the peripheral lamellæ. This probably depends upon the original distribution of the blood-vessels, which, if rami-

fying at very acute angles, will make their systems of lamellæ lie close together; but if ramifying at less acute angles, will leave interstices filled with distinctly lamellated intermediate bone-tissue. In order to render the formation of cortical bone easily understood, the following illustration is often used: take a number of matches, around each of which is twined a cord, and wind the cord around the bundle, the match representing the Haversian canal, the twines around each match the systems of lamellæ, and the twines around the bundle the peripheral lamellæ. This comparison holds good, of course, only for the case in which the intermediate bone-tissue is absent. The law, however, according to which the peripheral

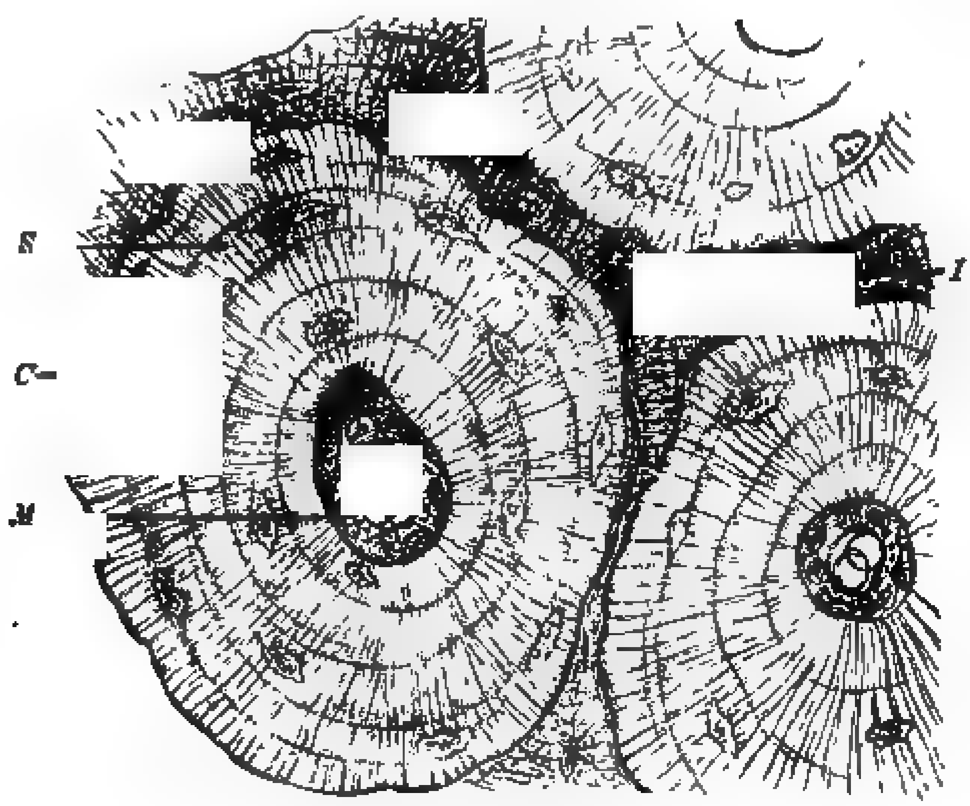


FIG. 88.—TIBIA OF A GROWN DOG. CORTICAL PORTION, TRANSVERSE SECTION. CHROMIC ACID SPECIMEN.

S, Haversian system of lamellæ, containing the bone-corpuscles, *C*, with their radiating offshoots. *M*, central medullary, so-called Haversian canal, containing a capillary blood-vessel; *I*, interstitial bone-tissue indistinctly lamellated. Magnified 500 diameters.

and the Haversian systems of lamellæ are formed, has not yet been explained.

With higher amplifications of the microscope each Haversian system proves to be composed of a number of concentric lamellæ, which are not perfect throughout the system. Both within and between the lamellæ, bone-corpuscles are visible with radiating offshoots, a number of which traverse the lamellæ, without being in direct connection with a bone-corpuscle. (See Fig. 88.)

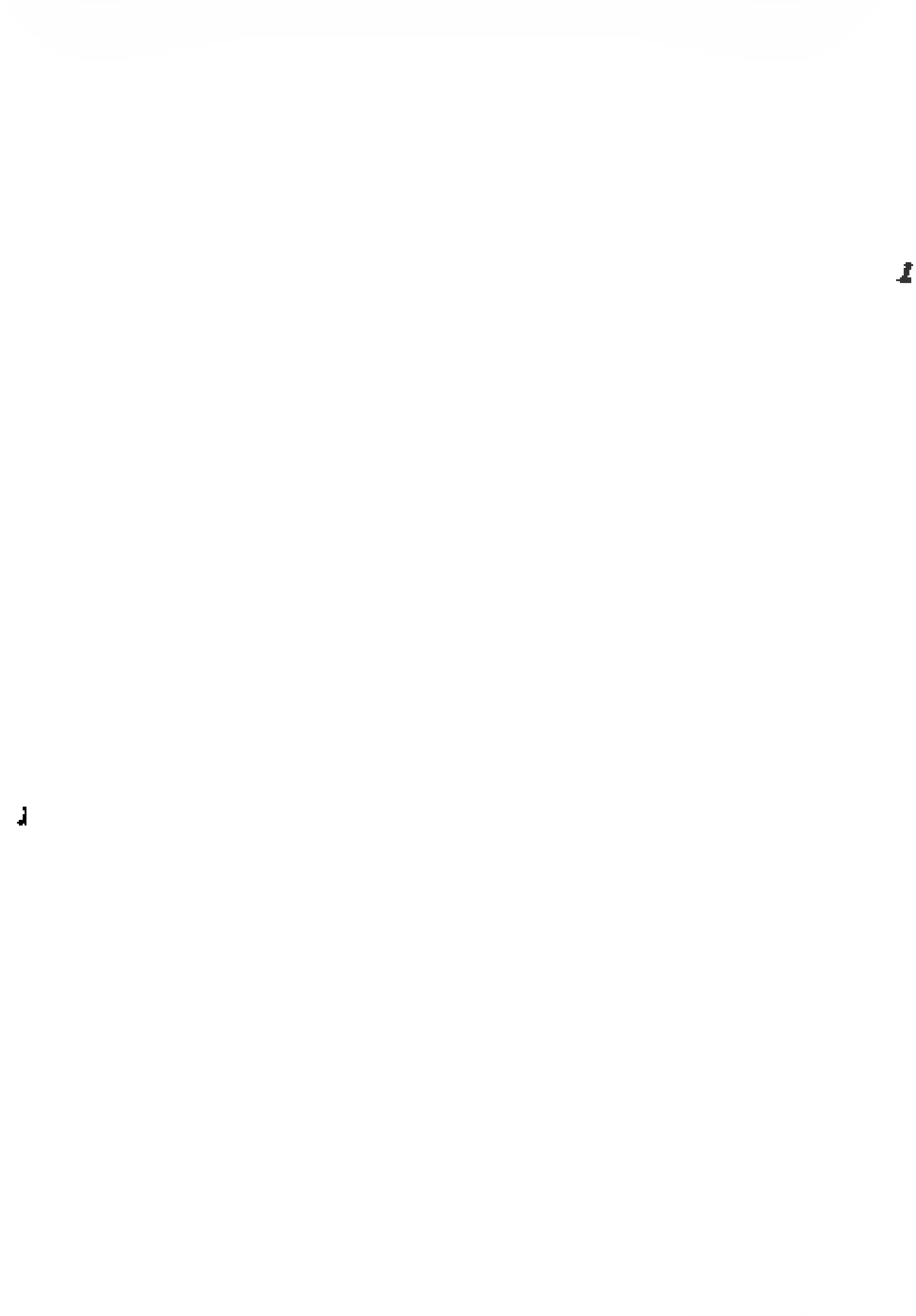
The center of the Haversian system is pierced by the medullary or vascular canal, which is of a varying caliber, according to the age of the individual, and contains, besides a certain number of medullary corpuscles, one or two central capillary blood-vessels. Whenever the extremity of the animal from which the shaft-bone was taken had been in a pendent position after death, the vessels are found filled with blood-corpuscles.

Longitudinal Sections are easily understood after the study of transverse sections. Here, too, the Haversian system is bordered by a fluting contour, due to the presence of globular territories of an early formation, and between the systems we find the intermediate bone-tissue, which in this situation, as a matter of course, will not exhibit lamination. In the intermediate portion we find the bone-corpuscles cut transversely, with most of their offshoots cut either obliquely or transversely, the latter being represented by a number of delicate dots.

In the Haversian system the lamellæ take a longitudinal course; within and between them are found the spindle-shaped bone-corpuscles, exhibiting, for reasons explained before, the greater bulk the nearer the periphery of the system. The offshoots of the bone-corpuscles emanating from their periphery, as well as from their polar projections, pierce the lamellæ at right angles. The central canal contains a varying number of medullary corpuscles, and in its middle one or two straight capillaries. Even with moderate powers of the microscope delicate filaments are recognizable, by which the offshoots of the bone-corpuscles connect with the medullary corpuscles, and the latter with the endothelial wall of the blood-vessel. (See Fig. 89.)

Periosteum. The investing fibrous connective-tissue layer of all bones, the periosteum as well as the cartilage, takes considerable part in the development of the osseous system. In human embryos of four to six months, the outermost layer of the periosteum consists of bundles of fibrous connective tissue, and between this layer and the cancellous bone there is a broad layer of medullary corpuscles, in continuity with the medullary formation in the spaces of the bone-tissue. From the outer fibrous portion of the periosteum oblique bundles of considerable density are seen to pass into the medullary spaces of the bone, and these bundles remain unchanged even after the compact portions of the bone have attained full development. Such bundles, faintly visible in chromic acid specimens, are termed "perforating or Sharpey's fibers" (described by Sharpey in 1856, but previously

'roja, in 1814). They traverse the outer peripheral system ımellæ, sometimes in the form of single cords, sometimes as oad reticulum, but often they are entirely absent.



ᶠIG. 89.—TIBIA OF A GROWN DOG. CORTICAL PORTION, LONGITUDINAL SECTION. CHROMIC ACID SPECIMEN.

S, Haversian system of lamellæ, containing the bone-corpuscles, C, with their transverse shoots. M, central medullary, so-called Haversian canal, containing a capillary blood-sel, I, interstitial bone-tissue. Magnified 500 diameters.

In fully developed bone the periosteum consists of two layers, outer fibrous portion being supplied with numerous blood-sels, which inosculate directly with the blood-vessels of the

bone-tissue, while the innermost portion, closely attached to the surface of the bone, is a dense ribboned layer, with a scanty supply of blood-vessels, but rich in elastic substance. This layer is often the seat of calcareous deposition, and owing to this fact its plastids assume irregular, jagged contours similar to those of bone-corpuscles. The calcified periosteum, however, is not true lamellated bone. It is often described under the name of the "*osteoid layer*." The periosteum is very thick at the points of the attachment of tendons and ligaments. The inner surface of the flat skull-bones, after the fifth or sixth year of life, is destitute of a periosteal investment proper. This can be clearly understood by the study of the development of these bones.

Blood-vessels. The bone-tissue, its investment,—the periosteum,—and its contents,—the medulla,—are plentifully supplied with blood-vessels. They enter the periosteum mainly at the points of attachment of the large ligamentous formations mentioned above. Arteries and veins are most abundant in the outermost portion of the periosteum, where extensive ramification of these vessels takes place. The arterioles enter the larger canals at the surface of the bones and branch into capillaries, which unite to form the efferent veins accompanying the arterioles. At the inner surface of the compact bone, also, there is a free anastomosis with the capillaries of the medulla. The medulla is supplied with numerous capillaries, arising from the so-called nutrient arteries of the bone, which pierce the cortical substance obliquely and split at acute angles, both within the canal and after entering the medulla. The veins collect the blood from tassel-like bundles of capillaries and accompany the afferent arteries. The epiphyseal portions of shaft-bones, besides the general medullary vessels, receive blood from the vessels which supply the articulations. The capillaries terminate, in the shape of loops, close below the articular cartilage. The veins in the bone-tissue are without valves, but as soon as they reach the surface of the bone, we find valves are present (C. Langer).

Lymphatics are not yet known to exist in the bone-tissue.

Nerves, both of the medullated and non-medullated variety, accompany the larger blood-vessels, but they are not abundant in the bone-tissue. In different places in the periosteum, Pacinian corpuscles are found.

The *medulla* of the bone is, in juvenile condition, a myxomatous tissue, at first of the medullary, later of the reticular variety (see pages 147 and 148), and, being freely vascularized, is

termed "*red medulla*." With advancing age the medulla is almost entirely transformed into fat-tissue, while the blood-vessels decrease in number on account of the large proportion of fat; it is then termed the "*yellow medulla*."

The Relation of the Systems of Lamellæ to the Blood-vessels.*

The cortical substance of the shaft-bones of a newly born pup is composed of trabeculæ, which form a reticulum, elongated in the longitudinal axis of the bone, the meshes being the medullary spaces. The width of a trabecula is about the same as the diameter of a neighboring medullary space. The trabeculæ are bone-tissue of a striated appearance, and contain flat bone-corpuscles in a concentric arrangement. In the medullary spaces we find the globular elements of the medulla closely packed together with ramifying blood-vessels, principally in the center. (See Fig. 90, and also Fig. 86.)

P

SM

T

M

Fig. 90.—Tibia of a New-born Dog. Transverse Section. Chromic Acid Specimen.

P, fibrous portion of the periosteum. *SM*, subperiosteal medullary layer; *T*, trabeculæ of bone; *M*, medullary spaces. Magnified 25 diameters.

In the compact substance of the bone of a dog about six months old, the bulk of bone-tissue several times exceeds that of the medullary tissue. We still meet with medullary spaces containing blood-vessels and globular elements. Far more numer-

* Translated from "Ueber die Rück- und Neubildung von Blutgefässen im Knochen und Knorpel." Wiener Mediz. Jahrb., 1873.

ous than medullary spaces, however, are the so-called "vascular canals"—*i. e.*, cylindrical or oval tubes, with one or two much elongated blood-vessels, and oblong or spindle-shaped medullary corpuscles. The larger the diameter of a medullary space or a vascular canal, the narrower, as a rule, is the surrounding bony layer; the broadest layers of lamellæ correspond to the narrowest vascular canals. The blood-vessels of the medullary spaces anastomose with those of the vascular canals by means of transverse and oblique branches; the vessels of the canals anastomose with each other, and with every vessel we find a varying thickness of lamellæ. (See Fig. 91.)

In the diaphysis of the tibia of a dog a little over a year old, the area of the bone-tissue surpasses that of the vascular canals, in

FIG. 91.—TIBIA OF A DOG, SIX MONTHS OLD. TRANSVERSE SECTION. CHROMIC ACID SPECIMEN.

M, medullary space, with a relatively small amount of surrounding lamellæ; S_1, narrow system of lamellæ around a medullary space; S^2, broader system around a vascular canal. Between the systems is the lamellated intermediate bone-tissue. Magnified 200 diameters.

a linear direction, six to eight times. In the compact bone, larger medullary spaces are found only in the vicinity of the central marrow-canal. The vascular canals are surrounded by broad systems of lamellæ, containing the bone-corpuscles in a concentric arrangement. Sometimes we meet, in transverse sections, with two smaller systems, each with a central canal, the two encircled by a common layer of an hour-glass shape. The interstices between the systems are filled by a non-lamellated bone-tissue, whose corpuscles are somewhat larger than those of the lamellæ, and irregularly distributed. The territories of such cor-

puscles are sometimes sharply marked. Into the intermediate bone-tissue we can also trace vascular canals—the lateral branches of the longitudinal vessels of the compact bone.

In the tibia of a dog several years old, the area of the bone-tissue surpasses that of the vascular canals by twelve or fifteen linear diameters. Large medullary spaces are found only near the central marrow-tube, while the rest of the cortex exhibits vascular canals of varying calibers, the larger of which contain some reticular connective tissue and fat-globules around the vessel. The parallel systems of lamellæ belong either to a single vascular canal or to two or three narrower systems which are surrounded by a large common system. The intermediate tissue is usually lamellated; in portions where lamellæ are wanting, semicircular or circular contours of territories are found surround-

I

S

O

FIG. 92.—TIBIA OF A DOG, TEN YEARS OLD. TRANSVERSE SECTION. CHROMIC ACID SPECIMEN.

S, system of lamellæ with a central vascular canal; *O*, system of lamellæ with a central bone-corpuscle; *I*, intermediate lamellated bone-tissue. Magnified 200 diameters.

ing small, bay-like spaces. Not infrequently we meet with systems of lamellæ, the centers of which are not occupied by a vascular canal, but by a bone-corpuscle.

Similar conditions are found in the tibia of a dog eight to ten years old, although the solid systems of lamellæ are still more numerous. The central marrow-tube is inclosed by a common lamellated bone-layer, while the layer between the periosteum and the bone is lamellated only in part. (See Fig. 92.)

The femur of the same animal is encircled by a broad, lamel-

lated layer beneath the periosteum, as well as at the border of the central marrow-tube. Where these layers are pierced by vertical vascular canals, such canals, as a rule, are surrounded by more or less perfect sheaths of lamellæ.

From these observations it follows that, independently of the general growth of the bone, the living matter stored up in the medullary spaces is the forming material of bone. The elements termed "medullary cells," as well as "osteoblasts," are transformed into bone-tissue, and in this way the lamellated layers of the bone become broader, and the medullary spaces, on the contrary, narrower. The systems produced by the contents of a medullary space surround smaller systems, the formation of which depends upon the single blood-vessels of the former medullary space, which now occupy the centers of the vascular canals.

All systems of lamellæ, therefore, are vascular territories,—as it were, stratified pillars,—the main longitudinal direction of which agrees with the course of the blood-vessels in their centers. From the main longitudinal course of this structure, branch systems, frequently in the oblique, rarely in the transverse, direction. The formation of non-lamellated intermediate bone-tissue also depends upon the blood-vessels.

Watching the contents of the vascular canals with high amplifications, I observed the following features:

In the bone of a dog about six months old, each vascular canal contains one or two blood-vessels, of varying caliber and of a straight course. I have several times seen nerves running along with the vessels, though my method of preparation was not favorable to the clearing up of nerve-tissue. The wall of the blood-vessel, as a rule, exhibits the simple structure of a capillary, with occasional spindle-shaped thickenings. The vessel is surrounded by a light rim, traversed by delicate grayish spokes, connecting the wall of the vessel with the neighboring spindle-shaped elements. The latter ensheath the perivascular space, either in a single flat layer or in several strata, and are also interconnected by short projections. Between the spindles and the bone-wall there is again a light rim, traversed by delicate offshoots, which directly connect the spindles with the offshoots of the bone-corpuscles.

In the tibia of a dog over a year old, I found similar vascular canals; besides numerous canals which, sometimes in places and sometimes in their whole length, contained only a capillary

vessel. I met with this arrangement most frequently in the older animals. Between the wall of the vessel and that of the bone there is always a light, narrow rim, crossed by projections of the neighboring bone-corpuscles, uniting with the wall of the blood-vessel. The rim is absent only when the blood-vessel is overfilled with an injection mass.

In the compact portion of shaft-bones and scapulæ of dogs, cats, and rabbits of middle or old age, I often encountered vascular canals, which were either constricted in an hour-glass shape or terminated in points. This condition was positively recognizable by the fact that, above and below the vascular canal, layers of bone-tissue (respectively bone-corpuscles) could be brought into focus. Closer examination of such vascular canals in longitudinal sections, as a rule, revealed the presence of but one blood-vessel. (See Fig. 93.)

Toward the pointed end the wall of the vessel became thickened, as if composed of spindle-shaped corpuscles, between which the caliber either narrowed suddenly or gradually, terminating close to a spindle-shaped body. In the caliber of the vessel red blood-corpuscles were occasionally present, and I repeatedly saw the injected mass penetrating the pointed end. The corpuscle which occluded the fine point of the vessel proved to be a bone-corpuscle, and in the direction of the vessel, at intervals, similar formations

FIG. 93.—HORIZONTAL SECTION OF THE SCAPULA OF A GROWN DOG. SPECIMEN DECALCIFIED WITH PYROLIGNIC ACID. [PUBLISHED IN 1873.]

C, capillary blood-vessel, containing a single row of red blood-corpuscles, the vessel pointed and solidified. *P*, elongated medullary corpuscle, and *B*, bone-corpuscle, both sprung from the solidified blood-vessel. Magnified 800 diameters.

were visible, separated from each other by finely granular or homogeneous shining masses.

The same condition was also observed in transverse sections. I found in the center of a system of lamellæ solid, finely granular corpuscles, which, in both an upward and downward direction, blended with the transverse cavities of bone or with the calibers of vessels. (See Fig. 94.)

The conclusions I arrived at are as follows: The material contained in the vascular canals is, with advancing growth, transformed into bone, leaving only the blood-vessel behind.

BC

FIG. 94.—TRANSVERSE SECTION OF THE INJECTED TIBIA OF A GROWN DOG. CHROMIC ACID SPECIMEN. A COMMON SYSTEM OF LAMELLÆ INCLOSES TWO SMALLER SYSTEMS. [PUBLISHED IN 1873.]

BV, the central vascular canal, with a capillary blood-vessel; *BC*, a central solid corpuscle sprung from a former blood-vessel. Magnified 800 diameters.

After a time, a transformation of the blood-vessels themselves to bone-tissue takes place by a solidification of the hollow protoplasma of the wall of the vessels, and thereupon a differentiation into bone-corpuscles and bony basis-substance.

DEVELOPMENT OF BONE.

It is a fact, well known for centuries, that the skeleton in the embryo is first formed of cartilage. The main question at all

times has been: How does bone arise from cartilage? A satisfactory answer to this question was impossible so long as the minute structure of cartilage was unknown, and, indeed, a full understanding of the process of ossification is of a very recent date.

Through the researches of Rathke, Reichert, Kölliker, and others, we know that there are bones which do not develop from cartilage, but from fibrous connective tissue, formerly thought to be a "blastema." All bones of the skeleton arise from preexisting cartilage, except the flat skull-bones—viz.: the squamous portion of the occipital and temporal bones, the parietal, frontal, and portions of the sphenoid bone, and the nasal, lachrymal, vomer, malar, palatine, and upper maxillary bones. The clavicle was in former times thought to be destitute of a cartilaginous basis, but recently it was found to be cartilaginous, at least at its extremities (M. Kassowitz). There is, however, a great similarity between the formation of the so-called "cartilaginous" bones and that of bones termed "covering." In all cartilaginous bones the formation of bone proceeds simultaneously both from the cartilage and from the perichondrium, the fibrous investing membrane.

The ossification of cartilage was first studied. In former times it was believed that, by the deposition of lime-salts, the cartilage was directly transformed into bone—the "cartilage cells" directly converted into "bone-cells." Observers were much puzzled over the formation of the "canaliculi," and Kölliker, in 1852, imagined that he had settled the matter by assuming that the cartilage-cells were transformed into bone-cells by a thickening of their walls, with a simultaneous formation of canaliculi, similar to the pore-canals of "wood-cells" of plants.

A new era was inaugurated in 1858 by H. Müller,* who, after very careful researches, came to the conclusion that the cartilage first breaks down into medullary tissue, and from this tissue bone is developed. H. Müller, however, admitted that a direct ossification of cartilage (metaplasia of authors) may also occur. Although he was ignorant of the fact that the whole medullary tissue giving rise to bone is an offspring of cartilage, the great merits of this accurate observer must always be recognized. *To-day we know that a direct transformation of cartilage or fibrous*

* "Ueber die Entwicklung der Knochensubstanz, nebst Bemerkungen über den Bau rachitischer Knochen." Zeitschr. f. Wissensch. Zoologie. Bd. ix.

tissue into bone never occurs; that between these two kinds of completed tissues the intermediate medullary, or embryonal tissue, stage is invariably present.

For the study of this highly interesting question the best subjects are the bones of human embryos, between the fourth and seventh months of intra-uterine life, or the correspondingly developed bones of newly born pups or kittens. These animals, at the time of birth, are, as I have already stated, advanced in development as far as human beings in the middle of intra-uterine life. Dogs and cats one year of age correspond in development of this tissue to human beings in the twentieth year of life, and dogs and cats ten to twelve years old are as far advanced in this regard as men of sixty years.

The phases of development of bone can, of course, be studied with greater ease in dogs than in human beings, and a number of facts obtained from the bones of animals have not as yet been established by investigation of human bones. All specimens must be preserved in, and partly or wholly decalcified by, a one-half per cent. solution of chromic acid; many of the blunders of former histologists, regarding development of bone, resulted from the examination of dry specimens.

Development of Bone from Cartilage.

In sagittal (antero-posterior) sections of shaft-bones of a human embryo, about five months old, we see that both ends of the future bone are composed of hyaline cartilage, containing many medullary spaces. With low powers of the microscope we recognize that the cartilage corpuscles are closely packed together in the outermost portions of the rounded extremities; next, the corpuscles are less crowded, but arranged, at regular intervals, in globular heaps, and gradually become arranged in rows, as the cartilaginous head slopes toward the middle portion, the future shaft. It is a mistake to suppose that these changes of shape and situation of the cartilage corpuscles are due to their own activity—that, as Virchow has expressed it, the corpuscles "direct themselves into rows." Before the third month of embryonal life we can easily ascertain the fact that, from the earliest stages of formation of cartilage, the rows are present in the middle portion. It is impossible to understand how cartilage corpuscles, being imbedded in a dense and tough basis-substance, could perform active locomotions without the basis-substance having been previously liquefied.

(a) Calcification. At a certain point, nearer the middle, in the younger embryo, the basis-substance is found to be the seat

of a calcareous deposition. This occurs first in the middle of the shaft, and gradually proceeds toward both extremities, varying considerably, both in time and extent, in different human embryos and in different animal embryos. In specimens decalcified by chromic acid, the basis-substance, which was the seat of a deposition of lime-salts, readily takes up the carmine stain. (See Fig. 95.)

The calcareous deposition occurs only in the broad masses of basis-substance b tween the territories of tl cartilage corpuscles, in co sequence of which an elo gated reticular frame is vi ble, which at first surroun the territories of the cartila corpuscles, and deeper belo in a nearly level line, it su rounds the spaces filled wi medullary corpuscles. Tl calcification is sharply d fined by pointed ends towa the unchanged cartilagino portion. In the deeper po tions of the calcified fran the first traces of new formed bone-tissue are n ticeable in the shape bright crescentic fields, a tached by their convex su faces to the calcified fram.. This investment of bone soon produces a continuous layer around the frame at its borders toward the medullary spaces.

BRYO, FIVE MONTHS OLD. SAGITTAL SECTION. CHROMIC ACID SPECIMEN.

C, rows of cartilage corpuscles in elongated groups, due to their territories, *F*, frame of calcified basis-substance, around which, in the lower portions, the first traces of bone-tissue are noticeable; *M*, medullary space, containing medullary corpuscles. Magnified 300 diameters.

In the cartilaginous heads of shaft-bones of human embryos, at a somewhat later period, a

deposition of lime-salts starts from the center of each head, independently of the calcified shaft. The frame of calcified basis-substance in this situation is of a roundish form, agreeing with the general shape of the cartilaginous head. In some cartilagi-

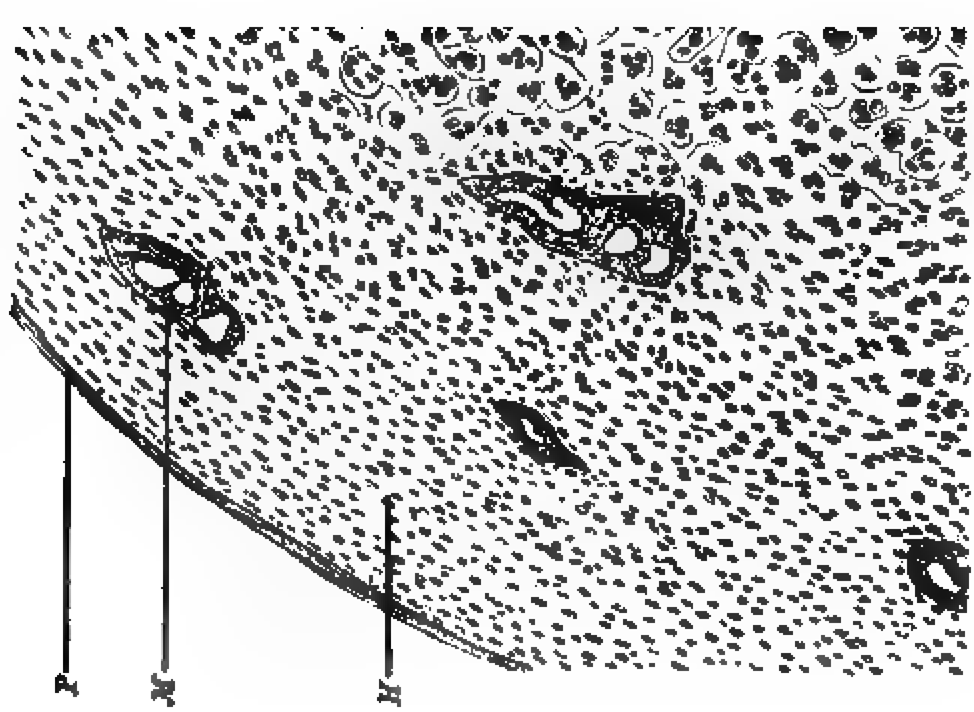


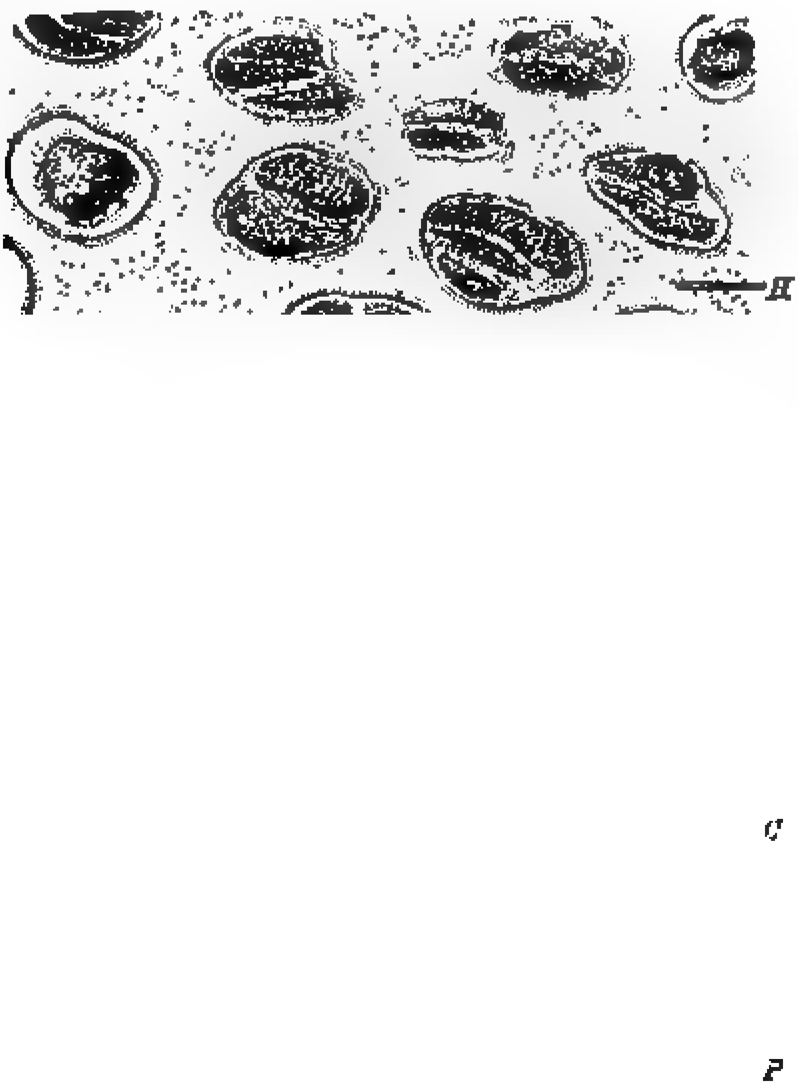
FIG. 90.—VERTEBRA OF A HUMAN EMBRYO, FIVE MONTHS OLD. HORIZONTAL SECTION. CHROMIC ACID SPECIMEN.

P, perichondrium; *H*, hyaline cartilage, with a number of medullary spaces, *M*, which contain the blood-vessels; *C*, calcified basis-substance of cartilage; *T*, trabeculæ of calcified basis-substance, inclosed by a layer of bone-tissue; *MC*, medullary spaces. Magnified 100 diameters.

nous heads of long bones, the calcification occurs at a very early period, f. i., in the vertebral ends of ribs; while in short bones the calcification, always starting from the center of the pre-

ed cartilage, is of a later date; f. i., in the vertebræ. (See 96.)

new-born pups, kittens, and rabbits these features are similar, though sometimes the calcification preceding the ation is wanting, even in shaft-bones (see, f. i., Fig. 98). wanting, as a rule, at the cartilaginous border of the plate scapula.



97.—VERTEBRAL EXTREMITY OF THE RIB OF A HUMAN EMBRYO, TEN WEEKS OLD. HORIZONTAL SECTION. CHROMIC ACID SPECIMEN.

, hyaline cartilage, with mostly multiple formations of corpuscles in the territories; cified frame of basis-substance; *P*, cartilage corpuscles with jagged offshoots, enlarged efaction of the basis-substance. Magnified 500 diameters.

Ve know that the calcification of cartilage is the first step in development of bone, and as this process takes place indeently in three portions of the shaft-bones, three nuclei of

bony tissue are formed—one in each epiphysis and one in the diaphysis. The outer portion of the epiphyseal cartilage is the articular cartilage proper; the cartilaginous portion between the epiphysis and the diaphysis is termed the diaphyseal or intermediate cartilage, which in human beings completely disappears about the twentieth year of life.

(b) Formation of Medullary Tissue. The cartilage corpuscles close above the place of calcification always have a coarse granular appearance, and are without a distinct nucleus. We understand from this that the bioplasson of the corpuscle has increased in amount, and thus begins a retrogression toward the juvenile condition. In the spaces surrounded by calcified basis-substance the cartilage corpuscles assume a very coarse granulation; many of them are nearly homogeneous, have a bright and vacuoled appearance, and are furthermore marked by radiating offshoots. (See Fig. 97.)

At the same time the cartilage corpuscles increase in bulk, also, by the addition of living matter, which, after the liquefaction of the basis-substance, simply re-appears from where it before was concealed. This *re-appearance* of living matter is indicated first by a somewhat coarser granulation of the basis-substance, and subsequently by the formation of new lines of demarkation, corresponding to the liquefied portion of the basis-substance. Even with moderate powers of the microscope all stages of the re-appearance of bioplasson are traceable, from a distinct granulation of the basis-substance up to the formation of fields exhibiting the features which in former times were termed "pale protoplasm." Such fields either surround the original cartilage corpuscle, or are joined to a part of the corpuscle. If the razor has struck the peripheral portions in a space surrounded by the calcified frame, only pale granular bioplasson is visible, and there will be seen basis-substance alone if the section reached the outermost portion.

The next stage is the splitting of the bioplasson masses into numerous smaller indifferent—*i. e.*, embryonal or medullary—corpuscles, each of which assumes a coarse granulation. It is obvious that at first only those embryonal corpuscles will appear which once themselves took part in the formation of the territory. By an increase of the bulk of their bioplasson these corpuscles become nucleated, and at first are finely, and later coarsely, granular. Small lumps of bioplasson may also show themselves, of a homogeneous appearance, a high degree of luster,

and a distinct yellow color. This indicates a new formation of living matter. In 1872, I named these solid lumps "hæmatoblastic" (see page 98), as I had observed the new formation of red blood-corpuscles arising from them. In 1873, I proved this condition to be the juvenile state of living matter in general (see page 51).

H. Müller asserted that many of the medullary corpuscles are the productions of the original cartilage corpuscles, and in this he was quite correct. But later observers, their number unfortunately being great, have disposed of the cartilage corpuscles by saying that they fade and perish, and that all medullary corpuscles are "leukocytes"—colorless blood-corpuscles, which have migrated from the blood-vessels of the medullary spaces, or of the perichondrium, through the cartilage and into the medullary spaces. There is no ground whatever for such assertions. To assume that leukocytes migrate through newly formed blood-vessels, which are not yet in connection even with the old vascular system, sounds whimsical enough. Further to insist, however, that leukocytes creep through the dense and unyielding basis-substance (for, at that time, nothing was known of "juice-canals"), is simply an absurdity. These hypotheses fall to the ground when we know that the basis-substance contains a large amount of living matter; that a liquefaction only of this basis-substance is required to free the bioplasson, from which, by its rapid growth and by the splitting of its lumps, new medullary corpuscles arise. The process, in short, is: *re-appearance, division, and new formation of bioplasson.*

That really the whole medullary tissue, filling the space inclosed by a calcified frame, is a production of both the cartilage corpuscles and the living matter in the surrounding basis-substance, is best illustrated by specimens where, without a preliminary deposition of lime-salts, the territories of cartilage tissue are immediately followed by medullary spaces. (See Fig. 98.)

Here we see, in certain territories of the cartilage, masses of medullary corpuscles in no way connected with the medullary spaces below. The spaces are exactly in a line with the territories directly above, and are filled with bioplasson lumps in all stages of development. (See page 46.) The centers of the masses exhibit a new formation, also, of red blood-corpuscles and blood-vessels.

(c) Formation of Red Blood-corpuscles and Blood-vessels.

Having ascertained the fact that red blood-corpuscles originate in places where a transformation of cartilage into bone takes place, I studied the development of blood-vessels in the same

FIG. 98.—FEMUR OF A NEWLY BORN PUP. TRANSITION OF THE EPIPH INTO THE DIAPHYSIS. NO CALCIFICATION OF THE BASIS-SUBSTA SAGITTAL SECTION. CHROMIC ACID SPECIMEN.

C, heaps of cartilage corpuscles, *H*, newly formed medullary corpuscles in a terri *M*, both cartilage corpuscles and basis-substance changed into medullary tissue, with t of newly formed blood-vessels. Magnified 500 diameters.

situation. My subjects for investigation were condyles of femur of pups and rabbits and the cartilaginous border of plate of the scapula of kittens.*

* Translated from "Ueber die Rück- und Neubildung von Blutgefä im Knochen und Knorpel." Wiener Mediz. Jahrb., 1873.

The hyaline epiphyseal cartilage of young animals, as is well known, is traversed by elongated medullary spaces, which contain, besides blood-vessels, including arteries, a large number of elements similar to those filling the medullary spaces of the bone. Such spaces also pervade the hyaline cartilage at the border of the plate of the scapula.

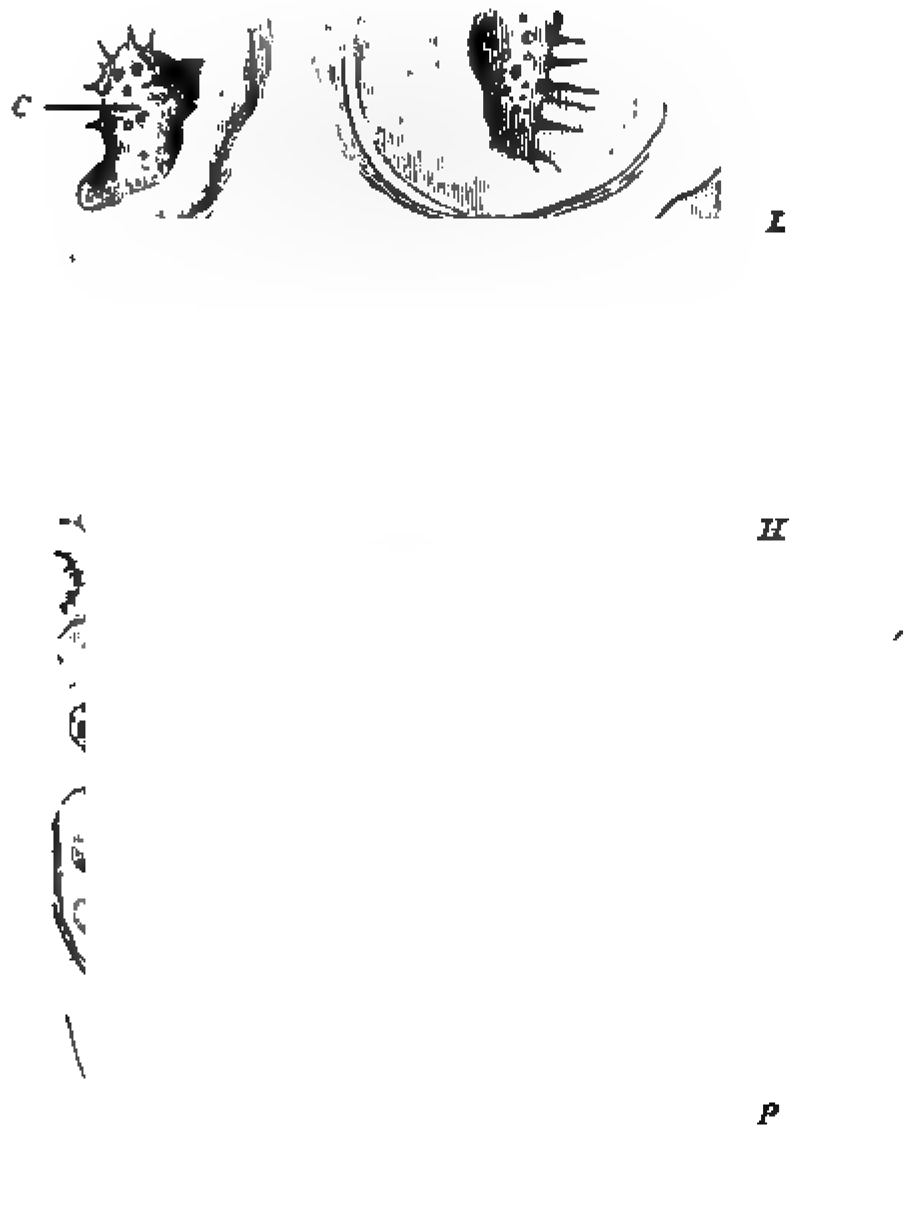


FIG. 99.—FROM THE CALCIFIED NUCLEUS OF THE CONDYLE OF FEMUR OF A DOG, SIX WEEKS OLD. FRESH SPECIMEN. [PUBLISHED IN 1873.]

C, coarsely granular cartilage corpuscles with offshoots, *H*, hæmatoblasts, in a club-like space, which is inclosed by delicate spindles and terminates in a solid point, *P*; *L*, calcified basis-substance. Magnified 800 diameters.

In the epiphyseal cartilage of the knee-joint of a newly born rabbit's femur, I found a radiating frame-work of calcified basis-substance, which, bordering a larger central medullary space, inclosed in its trabeculæ a number of cartilage corpuscles and

their non-calcified basis-substance. In the corresponding epiphyseal cartilage of a pup of five days there was no deposition of lime-salts present; while the same cartilage of a pup six weeks old contained a central semi-lunar calcareous nucleus, with its concavity directed toward the diaphysis, the trabeculæ of which inclosed a number of medullary spaces. The significance of this calcareous deposition was already known to Heinr. Müller.

FIG. 100.—FROM THE CARTILAGINOUS BORDER OF THE SCAPULA OF A KITTEN. FRESH SPECIMEN. [PUBLISHED IN 1873.]

C, yellow, bright, vacuoled cartilage corpuscles; *B* closed cartilage cavity, containing red blood-corpuscles, *M*, club-shaped spaces, holding red blood-corpuscles and hæmatoblasts. Magnified 800 diams.

Within the calcified portions of the cartilage metamorphoses occur in the medullary spaces, which, with a simultaneous solution of the calcareous frame, lead to the transformation of the cartilage corpuscles into blood-corpuscles and blood-vessels, as well as into medullary elements. (See Fig. 99.)

The process is the same in advancing development of bone-tissue at the borders of the diaphyseal or intermediate cartilage, at the border between the epiphysis and the articular cartilage, and at the border between the cartilaginous and the bony plate of the scapula. The central yellow and shining portion of the cartilage corpuscle is transformed into a vesicle, usually club-shaped, containing red blood-corpuscles. The swelled blunt extremity of the club is directed toward the periphery, while the more solid pointed end lies toward the larger central medul-

lary spaces. I also occasionally met with club-shaped formations, holding a light, finely granular, or an apparently structureless mass. (See Fig. 100.)

If several of these club-like formations, whether empty or holding red blood-corpuscles, were crowded together, they assumed the appearance of a cauliflower-like rosette, the same as after perforation of the calcareous wall between two neighboring cartilage cavities, when the spindle- or club-shaped formations come next to each other. The solid points or the walls of older formations of this kind became, after a time, hollowed out, and thus a varicose reticulum of blood-vessels arose which, from the very earliest period of their formation, contained red blood-corpuscles. Still later, the newly formed vessels may connect with older blood-vessels, and their contents be taken into the circulation.

*(d) Formation of Bone from Medulla.** In newly born pups, the formation of bone-tissue takes place within the medullary tissue from the medullary elements. The bone-tissue appears in the form of trabeculæ, which occupy the middle, between two blood-vessels or groups of vessels (see Fig. 86). The basis-substance of the trabeculæ is finely striated, and here and there is also indistinctly lamellated.

The transition of medullary into bone-tissue is demonstrated by the following forms:

In larger medullary spaces, between two blood-vessels, in the longitudinal section of the bone, we often meet with groups and tracts of spindle-shaped medullary elements. These are either homogeneous, bright, of a yellowish color, or granular, and supplied with vesicular nuclei, or they may be without nuclei. They are all separated from their neighbors by narrow rims. In transverse sections these tracts appear as roundish or oblong fields, composed partly of shining and partly of pale granular lumps, which are the cross sections of the spindles. We also encounter similar groups at the borders of already developed bony trabeculæ, and their general shape always corresponds to an elongated spindle or a rhomb.

From these groups the trabeculæ arise, by means of a deposition of lime-salts at regular intervals in one portion of the

* Translated from "Untersuchungen über das Protoplasma. IV. Die Entwickelung der Beinhaut, des Knochens," etc. Sitzungsber. d. Wiener Akad. d. Wissensch., 1873.

medullary corpuscles, while another portion remains unchanged and represents the bone-corpuscles. In accordance with the spindle shape of all medullary elements constituting a tract, the basis-substance assumes a *striated* appearance.

In growing animals, we often see rows of medullary corpuscles at the borders of bone-tissue toward the medullary space, which have been termed the "osteoblasts" by Gegenbaur.* That the elements of these rows really produce the bone was acknowledged

M

T

S

FIG. 101.—CORTICAL SUBSTANCE OF THE TIBIA OF A DOG, SIX MONTHS OLD. TRANSVERSE SECTION. CHROMIC ACID SPECIMEN.

M, medullary space filled with medullary elements, which at the border of the bone-tissue have assumed the shape of "osteoblasts." The center of the medullary space is occupied by a blood vessel. *S*, first trace of the formation of a Haversian system, composed of lenticular territories, which give to the circumference of the system a fluted appearance. *T*, globular territories, evidently the starting formations of new systems of lamellæ. Magnified 500 diameters.

also by later observers, as Waldeyer † and A. Rollett. ‡ A row of osteoblasts is evidently the basis of a future lamella of bone.

Before the infiltration with lime-salts takes place, a number of the osteoblasts are transformed into finely granular bodies,

* Jenaische Zeitschr. f. Mediz. u. Naturwissensch. 1864 and 1866.

† "Ueber den Ossificationsprocess." Archiv f. Mikroskopische Anatomie. Bd. i. 1865.

‡ "Handb. d. Lehre von den Geweben." Herausg. v. S. Stricker.

destitute of nuclei, the connection of which with each other and with neighboring formations of the same nature is established by the delicate spokes which traverse the intervening light rims. After the infiltration with lime-salts is accomplished, an optical differentiation of the lamella into single "osteoblasts" is possible in exceptional instances, when the lamella has the appearance of being composed of polygonal fields. More frequently the optical boundaries of the single osteoblasts fade, and only central portions of the lamella remain intact in the form of bone-corpuscles. In this case, therefore, a number of protoplasmic bodies have coalesced into a slightly curved lenticular formation, a tissue-unit, the center of which is the bone-cell.

F

B

FIG. 102.—VERTEBRA OF A HUMAN EMBRYO, FIVE MONTHS OLD. HORIZONTAL SECTION. CHROMIC ACID SPECIMEN.

M, medullary space, with central blood-vessels and medullary tissue; *B*, first-formed globular territories, containing one or two central bone corpuscles, with radiating offshoots. The territories lie against the trabecula of the original calcified basis-substance of the cartilage, *F*. Magnified 500 diameters.

A number of such lenticular territories constitutes a single *lamella* of bone-tissue.

In the compact and the so-called intermediate substance of

shaft-bones of growing and adult animals, we encounter numerous circular fields, containing one or more bone-corpuscles. We also find within the medullary spaces globular bodies, containing several nuclei, or only a number of nucleoli, sometimes exhibiting a uniform coarse granulation, due to the large points of intersection of the living matter. These masses, termed "myeloplaxes" by their discoverer, Ch. Robin, are likewise the predecessors of bone formation, as I demonstrated in 1872.* Here a portion of the protoplasma is transformed into basis-substance, which at once becomes calcified, while the central portion is not changed into basis-substance, and remains as the bone-corpuscle or the bone-cell. (See Fig. 101.)

We often find lenticular, multinuclear masses in the shaft-bones of growing animals, not only in the epiphysis at the borders of medullary spaces, but also in the vascular canals of the diaphysis. Such masses are separated from their neighbors by light rims, but also connected with them by delicate spokes of living matter. These are the first traces of a third kind of tissue-units of the bone, the *bone-globules*, which are known by Virchow to be the cell-territories proper. Each of these originates from a multinuclear mass, and each contains one or more bone-corpuscles.

Formations of this globular variety are met with also in the calcareous nucleus of the epiphyseal cartilage, at the ossifying border of the diaphyseal or intermediate cartilage, "and in the centers of calcification of short bones." [The last words are newly added.] (See Fig. 102.)

The multinuclear bodies, which have sprung from medullary elements, are, therefore, the regular bone-formers, appearing first around the trabeculæ of the calcified basis-substance of cartilage, and later independently of other formations. *It depends entirely on the original shape of the medullary lumps, whether the bone-tissue assumes a striated, lamellated, or globular structure.*

Bone, therefore, as well as all other varieties of connective tissue, is a product of the medullary or embryonal tissue, the elements of which either split into delicate spindles, resulting in the formation of a striated basis-substance, or coalesce into lenticular masses, a number of which unite in the construction of a lamella, or else coalesce into globular masses, from which arise the globular territorial formations of the bone-tissue.

* "Studien am Knochen u. Knorpel." Mediz. Jahrb., 1872.

The Process of Ossification in Birds. By L. Schöney.*

My observations were made on a number of chickens and pigeons of different ages, the cartilages of the knee-joint, preserved and decalcified in chromic acid, being my subjects of study. Sagittal sections through the knee-joint of birds demonstrate that the bulk of the hyaline cartilage decreases with age, and that a transformation of cartilage directly into medullary elements and indirectly into bone takes place only in young animals. In older ones completed bone-tissue bounds the cartilage, and in old pigeons the medullary spaces of the bone produce elongations which at a certain height penetrate the cartilage.

In sagittal sections of young animals, we see with low powers of the microscope the following: At the articular surface, and near the perichondrium, elongated, spindle-shaped cartilage corpuscles are found, which gradually change into globular, nucleated corpuscles. The latter are met with in the middle portion of the cartilage, which is pervaded by medullary spaces, containing blood-vessels. The layer of the globular, nucleated corpuscles is followed by a narrow layer, in which there are small, flat cartilage corpuscles of a yellow-red color, bounding the district of calcification. The calcified basis-substance produces a pretty frame-work, which blends with the first-formed trabeculæ of bone-tissue, surrounding the medullary spaces of the epiphysis.

With higher powers, we ascertain that the calcareous frame penetrates the basis-substance of the unchanged cartilage by means of pointed ends. Within the frame the cartilage corpuscles are distinctly recognizable. In many places the trabeculæ of bone are directly attached to the calcareous frame, the feature distinguishing these formations being the bone-corpuscles of the trabeculæ. The medullary spaces are filled with globular, oblong, or spindle-shaped medullary elements; besides these we often encounter protoplasmic masses of varying size, either multinuclear or destitute of nuclei, but uniformly granulated. Spindle-shaped elements are most prevalent in the center of the medullary space, where the spindles are in connection with blood-vessels. (See Fig. 103.)

The formation of medullary spaces is best studied in horizontal sections. First we recognize that at certain intervals a dissolution of the calcified basis-substance of cartilage takes place. It is true that the direct transformation of the cartilage into free protoplasma, with the formation of bright lumps, filling the medullary spaces, cannot be directly observed, but we may readily deduce such a transformation, as all medullary spaces in the neighborhood are inclosed by a calcified cartilage tissue, and the calcareous frame projects into the medullary space, as if broken.

The transition of cartilage into medullary elements is initiated by the deprivation of a cartilage tissue unit or territory of its lime-salts. Adjoining the zone of decalcified cartilage there is found a layer of protoplasma consisting of numerous glistening lumps. These lumps are surrounded by a light narrow rim, which is seen occasionally to be traversed by filaments. The lumps bear a close resemblance to like formations in mammals, which have been described under the name of "hæmatoblasts." The char-

* Extracted from the essay of Dr. L. Schöney, in New York. "Ueber den Ossificationsprocess bei Vögeln." Archiv f. Mikroskop. Anatomie," Bd. xii., 1875. For the second part of this publication, see page 103.

acter of many places, one of which I have illustrated, forces us to the conclusion that not only the cartilage corpuscles, but the whole mass of living matter stored up in the basis-substance of the cartilage, participates in the formation of medulla. No other interpretation is admissible, for a sudden transition of an apparently structureless basis-substance into a protoplasmic

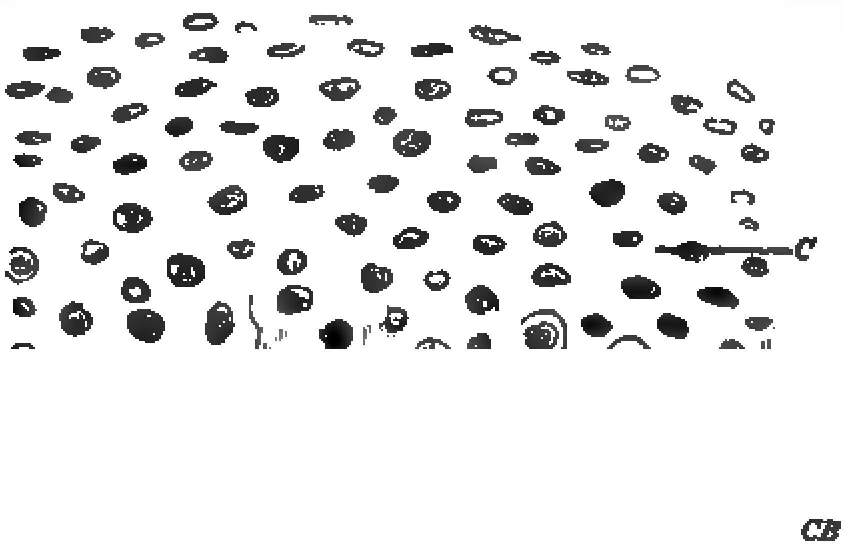


FIG. 103.—ARTICULAR CARTILAGE OF A YOUNG CHICKEN. SAGITTAL SECTION. CHROMIC ACID SPECIMEN.

C, hyaline cartilage ; *CB*, calcified basis-substance of hyaline cartilage; *M*, medullary space ; *B*, trabeculæ of newly formed bone. Magnified 450 diameters.

mass takes place without a trace of an intervening division of the cartilage corpuscles. (See Fig. 104.)

At the border where the cartilaginous basis-substance is dissolved, we not infrequently meet with cartilage corpuscles, partly imbedded in the basis-substance, partly freely projecting into the previously formed medullary space, but I never saw marks of division of such corpuscles. Instead of

assuming, as is generally done, that a division of cartilage corpuscles takes place, it would be better to hold that, in the protoplasma set free by liquefaction of the basis-substance, there is at certain intervals a new formation of living matter, which results in the formation of the compact, glistening lumps. The multinuclear protoplasmic bodies, the "myelopaxes," according to this view, are simply freed territories of the cartilage tissue, and we can easily understand that occasionally a number of such territories coalesce into a common layer, before a further differentiation occurs.

Unquestionably, the cartilage tissue is directly transformed into medullary tissue. The question how bone-tissue arises from medullary tissue is answered by the careful study of places where newly formed bone is closely attached to calcified cartilage. Here we notice a regular layer of finely granular osteoblasts

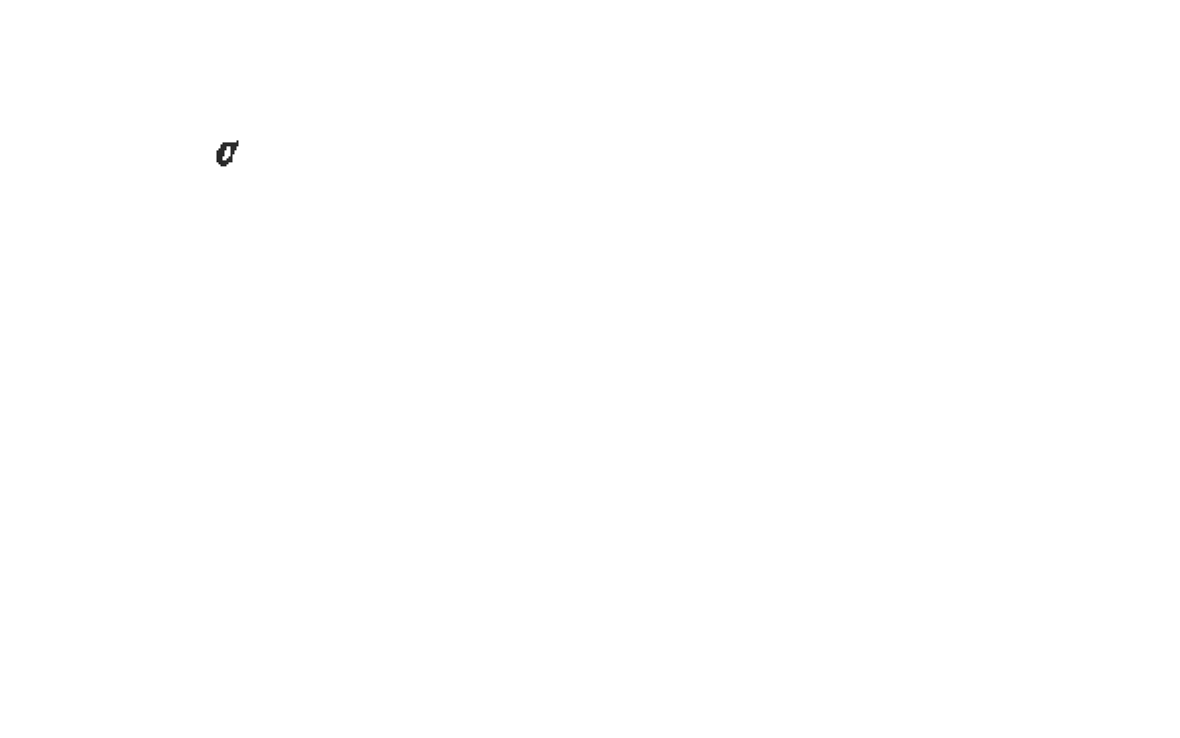


FIG. 104.—KNEE-JOINT CARTILAGE OF A YOUNG CHICKEN, CLOSE TO THE BORDER OF OSSIFICATION. HORIZONTAL SECTION. CHROMIC ACID SPECIMEN.

C, calcified frame of basis-substance of hyaline cartilage; *H*, zone from which the lime-salts have been dissolved, *M*, newly formed medullary space. Magnified 700 diameters.

between the decalcified basis-substance of cartilage and the newly formed bone. We can also trace every transition of free, uninfiltrated osteoblasts from the first steps till they finally fade in the basis-substance. The delicate granulation of the new osteogeneous basis-substance indicates that in the formation of bone the structure of the osteoblasts has not been completely lost.

The bone of birds is essentially constructed like that of mammals. We find systems of lamellæ around vascular canals; we also find in the cavities of the basis-substance the bone-corpuscles, with their characteristic stellate offshoots. How far the presence of living matter within the basis-substance of the bones of birds corresponds with that of the mammal, further researches must reveal.

Development of Bone from Fibrous Connective Tissue.

A great part of the skeleton grows from fibrous connective tissue, independently of preformed cartilage. The strict distinction which in former times was made between "cartilaginous" and "covering" bones (see page 237) can be upheld only to a certain extent. It is true that in the production of covering bones no preformed cartilage participates, yet all the other bones of the skeleton, including the flat, the short, and the shaft bones, obtain only a part — viz., their cancellous portion, from preformed cartilage. Their cortical or compact portion is formed entirely from periosteum. Many observers have noticed, in different places beneath the periosteum, cartilaginous layers; but no importance need be attached to the presence of such a layer, as the formation of bone-tissue is materially similar, whether it is developed from cartilage or from fibrous connective tissue.

In the shaft-bones of human embryos ten to twelve weeks old, when no trace of calcification is yet noticeable, the cartilage is found to be surrounded by a delicate fibrous investment,—the perichondrium,—between which and the surface of the cartilage there is a broad layer of medullary tissue. From the latter tissue arises the future cortex, simultaneously with the calcification and ossification of the cartilage in the center. At the fourteenth week there is already a distinct cortex around the diaphysis, at the same time when the transformation of the cartilage into medulla and cancellous bone has also commenced in the central portion of the diaphysis. The cortex and the calcified cartilage occupy about the same height, the middle portion always being the starting-point for their formation. Both portions, however, at first exhibit the cancellous structure, while the formation of regular lamellæ begins to appear much later.

The first-formed cancellous bone of the cortex has a striated structure agreeing with the spindle-shaped territories of the mother-tissue — the periosteum. The first-formed cancellous bone of the center, on the contrary, is composed of globular territories corresponding to the globular territories of the mother-tissue — the cartilage. It is only on this ground that we are able to understand the difference in the structure of the earliest-formed bones, the formation of "perforating fibers," and the vascular system of the cortex. The law, however, according to which the peripheral lamellæ and the Haversian lamellæ are formed is not known. Probably there are three main layers in

the original periosteum, the fibers and blood-vessels of which stand at right angles to each other.

The formation of bone from fibrous connective tissue is best studied in the skull of the human embryo, at about the fourth month of development. (See Fig. 105.)

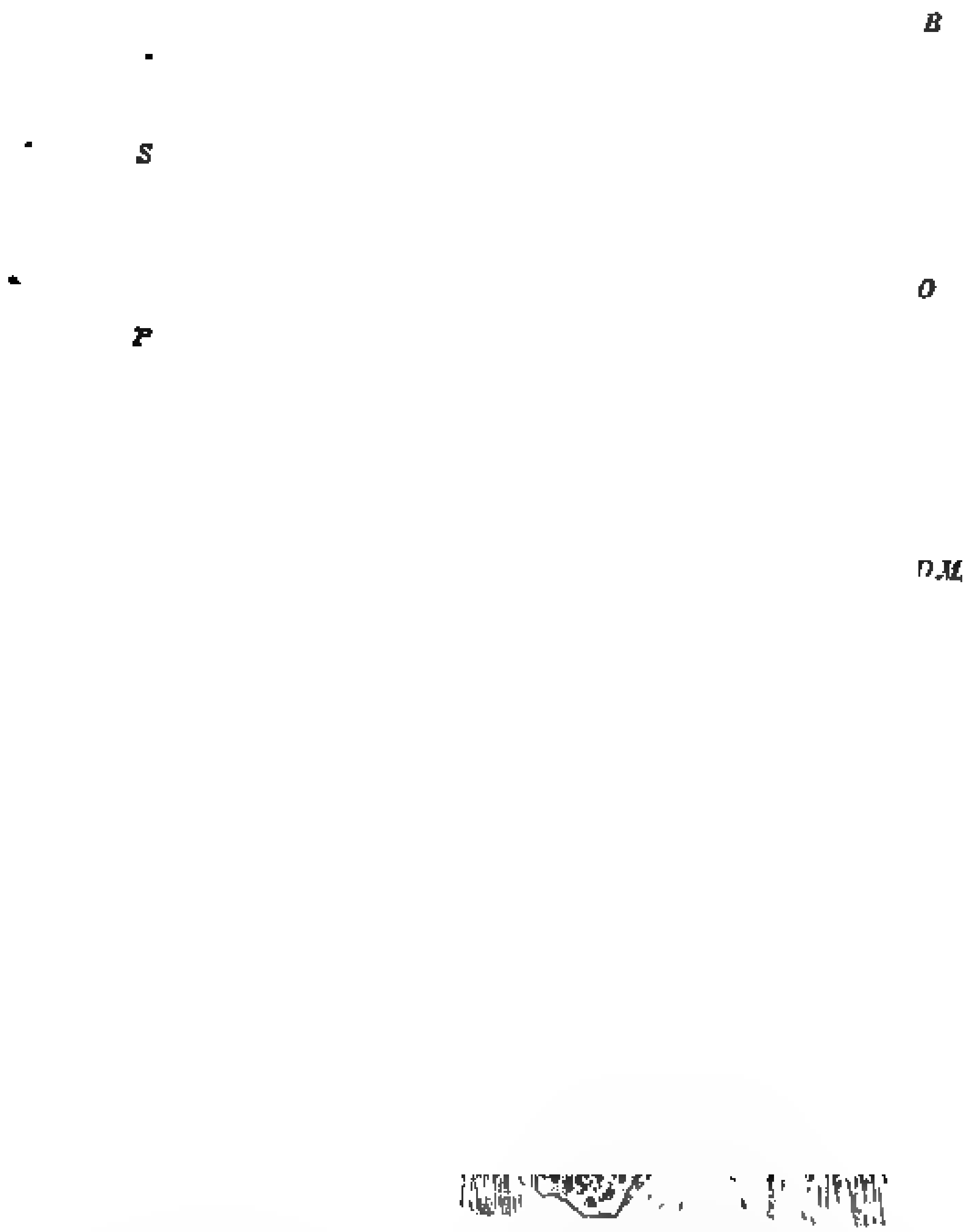


FIG. 105.—SKULL OF A HUMAN EMBRYO, FOUR MONTHS OLD. HORIZONTAL SECTION. CHROMIC ACID SPECIMEN.

[illegible], muscle-layer of the scalp, *SM*, submuscular loose, freely vascularized connective tis- [illegible] *P*, dense connective tissue of external pericranium, *B*, first-formed trabeculæ of bone, *O*, [illegible]er of osteoblasts, attached to the trabeculæ, *DM*, dense connective tissue of internal peric[illegible]ranium—the future dura mater. Magnified 100 diameters.

We observe in the middle of a layer of fibrous connective tissue medullary corpuscles in longitudinal tracts (if cut transversely); we see that a number of such corpuscles coalesce in order to be transformed into basis-substance, which almost instantaneously becomes infiltrated with lime-salts. In this way

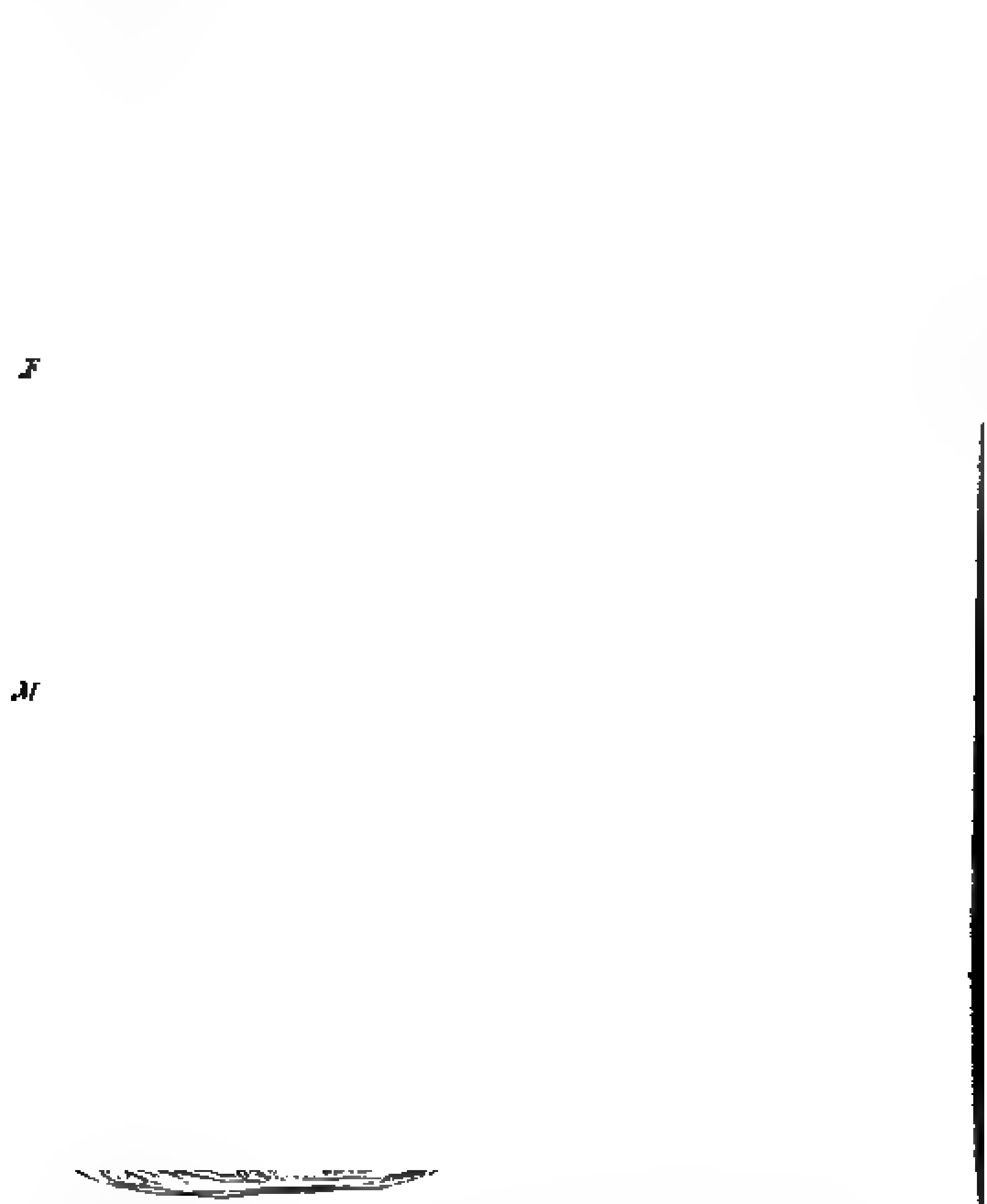


FIG. 106.—SKULL OF HUMAN EMBRYO, FOUR MONTHS OLD. HORIZONTAL SECTION. CHROMIC ACID SPECIMEN.

F fibrous connective tissue of the pericranium; *M*, medullary space, with central blood-vessel; *B*, first formed trabecula of bone; *O*, row of osteoblasts; *C*, medullary corpuscles of the inner pericranium, infiltrated with lime-salts. Magnified 500 diameters.

trabeculæ of bone, with large and irregular bone-corpuscles, are formed between two layers of fibrous connective tissue, the outer of which is the future external, the inner the future inter-

l, pericranium. Five or six years after birth, the latter separates ›m the skull-bone and furnishes the dense investment of the ain, the dura mater. The first trace of a bony formation is variably found in the middle field between two blood-vessels, those localities, therefore, where there is the least nutrition, in e same manner in which the bony formation arises from carti-ge. The further growth of the trabeculæ always proceeds from e medullary tissue, particularly from the medullary corpuscles, ually of only one side, lying close to the border of the tra-cula. This process is identical with that of the growth of beculæ which have arisen from original cartilage.

For studying the details of the formation of bone from fibrous nnective tissue, with high amplifications of the microscope, the st subject also is the skull of a human embryo. (See Fig. .)

We observe at first that, from single medullary corpuscles, en grouped together, basis-substance originates, which is at e infiltrated with lime-salts. The embryonal condition is next stablished in these corpuscles by liquefaction of the basis-ostance, and they are again plastids, which may afterward alesce to form a larger mass, the first indication of a territory, hibiting a central bone-corpuscle. Still later, a number of h masses, always through the intervening condition of uncal-ied medullary tissue, coalesce, and a trabecula arises, with a mber of large and irregular bone-corpuscles, with their stellate shoots. It makes no difference whether a blood-vessel is pres-t from the beginning of the process, or whether it is formed terward; it will always occupy the center of a medullary ace. Upon close observation of the distances between the ngle bone-corpuscles, we are satisfied that at first from only a ngle corpuscle, and later from a limited number of medullary orpuscles, calcified basis-substance arises in the same manner, herefore, in which the myxomatous basis-substance is formed see page 148). At first, no distinct territories are present; these re only recognized later, when the lamellated structure begins to appear.

Obviously, the originally formed bone-tissue is not perma-nent. The bony trabeculæ in turn are repeatedly reduced by liquefaction of their basis-substance to the embryonal or medul-lary condition, and new bone-tissue continues to form up to the ime of full development of the body. A continuous absorption nd reformation of bone is probably going on throughout life.

This, to some extent, is influenced by certain conditions—for example, on the skull-bones by the growth of the brain, both in a progressive and regressive way (Virchow). The regression is shown by the absorption in advancing age, producing the thinning of the bones so characteristic of the senile skeleton.

The Growth and Retrogression of Bone.

In the light of my researches, continued for ten years, the theory of an interstitial growth of the bone is no more tenable than is the interstitial growth of any other tissue. Basis-substance, once formed, cannot increase in bulk by simple expansion. The observation that the bone-corpuscles in the old are farther separated than in the young is no proof of an interstitial growth, since Steudener has demonstrated (see page 220) that the peripheral portion of each bone-corpuscle in advancing age is transformed into basis-substance. *New tissue forms exclusively from embryonal or medullary tissue, and an already formed tissue must return to its embryonal condition, by liquefaction of the basis-substance, before a new tissue can arise. An augmentation of the bulk of a tissue can take place only by new formation of the living matter of the embryonal corpuscles, that is, an increase of the number of the embryonal corpuscles.*

This law was first, though incompletely, established by H. Müller, in 1858; it was asserted as to the growth of bone-tissue by L. Ranvier in 1865, and announced to be a universal law for all tissues by myself in 1873. The process of inflammation, first accurately studied by S. Stricker, also illustrates the law. Inflamed tissue, according to S. Stricker, returns first to its embryonal condition before new formation arises.

We are indebted to A. Kölliker's accurate researches * for the discovery that every growing bone on its surfaces exhibits regularly recurring "planes of resorption" (Resorptions-flächen). The bone to the naked eye looks rough, as if corroded; under the microscope the bone-tissue proves to be spongy, provided with bay-like erosions or excavations, which, as a rule, contain multinuclear bioplasson masses. Kölliker maintains that these bodies are growing into the bone-tissue from without, and that they actually absorb and destroy the bone structure. For this reason

* "Die Normale Resorption des Knochengewebes u. ihre Bedeutung für die Entstehung der Typischen Knochenformen." Leipzig, 1873.

he proposed for their designation the rather alarming name of bone-breakers—"osteoklasts."

The multinuclear bioplasson bodies were first described by Robin under the title of "myeloplaxes." Virchow termed the same formations "giant-cells"; English authors, "myeloid cells." They are, as I demonstrated in 1873 (see chapter on inflammation), the bioplasson formations of the bone-tissue itself, the territories of the basis-substance of bone, either after decalcification and liquefaction of the basis-substance, or before the formation of a territory of bone. (See Fig. 107.)

G

M

FIG. 107.—SURFACE OF THE SCAPULA OF A KITTEN. CHROMIC ACID SPECIMEN.

C, calcified lamellated bone, with bone-corpuscles, G, a single territory of bone-tissue liquefied, resulting in the formation of a multinuclear plastid; M, coalesced masses of multinuclear plastids. Magnified 600 diameters.

We see these bodies, not only in medullary spaces of all juvenile bones, but also in the planes of absorption at the surface of growing bones, beneath the periosteum, and in inflamed bone. They certainly are not extraneous, but the medullary corpuscles themselves, coalesced into larger layers for the production of

territories in forming bone. An already formed bone, being deprived of its basis-substance either by advancing growth or by the inflammatory process, at once falls back into the bioplasson stage, and exhibits first bioplasson territories, which later again divide into medullary corpuscles. All territories and all medul-

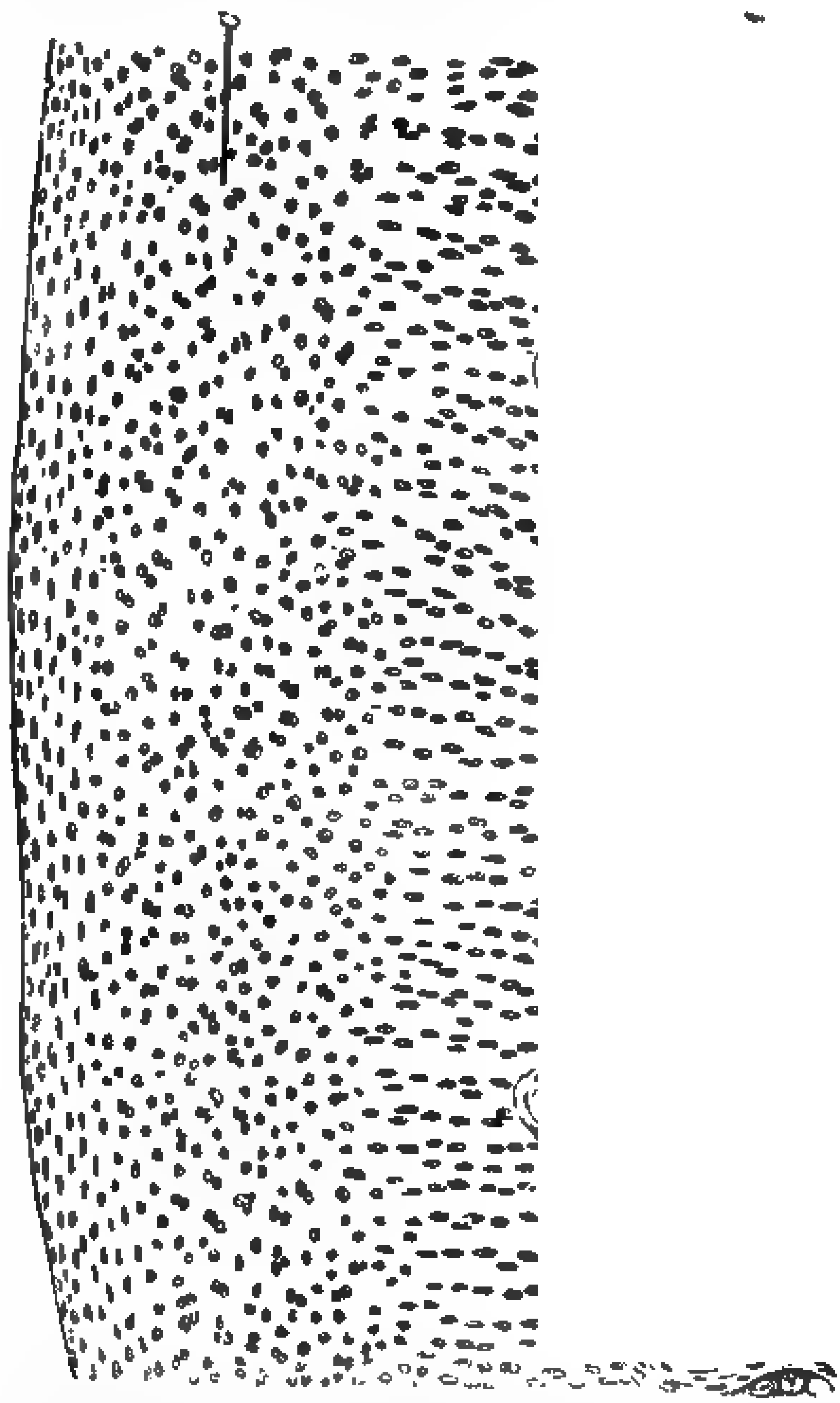


FIG. 108.—ARTICULAR EXTREMITY OF THE FEMUR OF A DOG, TWELVE YEARS OLD. SAGITTAL SECTION. CHROMIC ACID SPECIMEN.

C, hyaline cartilage; B, zone of lamellated bone; M, marrow spaces, filled with vacuoled fat-globules. Magnified 100 diameters.

lary plastids remain interconnected by means of delicate filaments, which traverse the surrounding light rims, and such a connection is also established with the adjacent reticulum of bioplasson of unchanged bony basis-substance. In these masses we usually observe all stages of development of bioplasson, from the solid

homogeneous lump into a nucleated plastid, and from this into plastids with nucleoli only, and finally into granular plastids, destitute of nuclei and nucleoli. (See page 55.)

The interpretation here given does not, however, explain the appearance of such bioplasson bodies in dead bone. Ivory sticks, driven into living bone for surgical or experimental purposes (Billroth), and necrotic bone likewise, exhibit bay-like excavations at their surfaces, filled with multinuclear bioplasson masses. Obviously, these masses could not have originated from the dead ivory and the necrotic bone. Their bay-like excavations are explicable, as Virchow has already shown at length, by assuming in them a decalcification and liquefaction of the basis-substance, corresponding with the territories; and, since Ziegler has demonstrated that even between two thin glass plates, placed into the subcutaneous tissue of animals, migrating plastids accumulate and coalesce into multinuclear masses, a similar process may be admitted for the filling of these bay-like excavations.

That the multinuclear bodies really arise from the liquefied living bone-tissue itself I have ascertained in provisional teeth, the erosions of which were studied, in the last few years, in my laboratory, by Dr. Frank Abbott; and there can be no doubt that they are a growth of medullary corpuscles from without, whenever the bone is deprived of its life.

Cartilage with advancing age gradually decreases in amount; in the aged we find only a thin layer of articular cartilage. In old dogs, the thin layer of the articular cartilage, toward the marrow spaces, is bordered by a well-marked lamellated zone of bone. (See Fig. 108.)

That the bone-tissue itself does decrease in bulk with advancing age is best illustrated by the toothless jaws of the aged. The cause of this absorption and atrophy of the bone-tissue, invading both the cancellous and compact structure, has not yet been elucidated.

VIII.

MUSCLE-TISSUE.

MUSCLE, the motor apparatus proper, is a formation of living matter in a reticular arrangement. The points of intersection in smooth muscle are irregularly scattered; in striated muscle, they are arranged with great regularity in the so-called sarcous elements. The connecting filaments are extremely delicate, allowing slow but, considering the bulky formations of muscle, powerful contractions of the living matter.

Muscle is constructed on the plan of an amœba, or that of any other plastid. The difference is that the points of intersection of the living matter in the amœba are small and irregularly distributed, while in muscle the nodules of the reticulum are large and more or less regular in their arrangement. The fluid contained in the meshes of the reticulum in the amœba corresponds to the muscle fluid between the rows of sarcous elements. Contractility is inherent in the amœba and every plastid; therefore, also in muscle, independently of nervous influence. The independent contractility of muscle was proved by J. Müller, in 1834, after division of the nerves, and by Claude Bernard, in 1857, after abolishing the action of the motor nerves by curara. The enlargement of the nodules of living matter, the shortening of the connecting filaments, and the narrowing of the mesh-spaces produces the contraction in the amœba, as well as in the muscle (see page 29). The difference is that, while in the amœba one portion of the body is in contraction, the other, on the contrary, in extension: in all highly developed animals one muscle, or a group of muscles, is in the state of contraction, while

another muscle, or a group of muscles, is in that of extension. Muscles which simultaneously work in such an opposite manner are termed "antagonists."

Muscle formations are of two varieties. In the tissue of the *unstriped, smooth, or involuntary muscle* the bioplasson is stored up, without much regularity, in comparatively small spindles. In the tissue of the *striped or voluntary muscle* the bioplasson is distributed regularly in the shape of sarcous elements, in relatively large spindles.

1. Smooth or Unstriped Muscle.

Smooth muscle is constructed of spindle-shaped plastids, which are usually nucleated, and are held together in bundles by means of a delicate cement-substance, surrounding each spindle. Ensheathing the bundles there is a delicate layer of fibrous connective tissue, the perimysium. The muscle nature of these spindles was discovered by A. Kölliker in 1847.

The spindles vary greatly in size. Very small spindles are found in the skin and large arteries, medium-sized spindles in the muscle-layers of the mucous membranes, and very large spindles in the pregnant uterus. In all instances the separating cement-substance can be stained brown by nitrate of silver, and the brown line thus produced is pierced at right angles by delicate light lines which correspond to the minute transverse spokes interconnecting all spindles. The spokes are visible with high powers of the microscope, without the addition of a re-agent. The granules of the spindle are, as a rule, coarse, so as often to conceal the central oblong or rod-like nucleus, which, however, is easily seen in transverse sections. The granules not infrequently exhibit a partially regular arrangement, especially toward their tapering ends, which produces an appearance resembling the sarcous elements of striated muscles. The outlines of the spindle are smooth and regular when in a state of rest; but they become slightly scalloped by contraction, when the body of the spindle is shortened and broadened.

The bundles of smooth muscles of the skin are most abundant in the region of the nipple and in the scrotum. They run in oblique directions, interlacing sometimes at acute angles. The oblique section of a bundle is characterized by short spindles;

the transverse section by disks, exhibiting, when the razor has passed through the middle of the spindle, the bright central nucleus. (See Fig. 109.)

Bundles of smooth muscle are often found connecting into a reticulum—f. i., in the scrotum, the labia majora, the prostate gland, the urinary bladder. The bundles are spread in flat layers throughout all larger tubular formations of the alimentary and the genito-urinary tract. We find in these tubes at least two layers, of which the one nearest the epithelial sur-

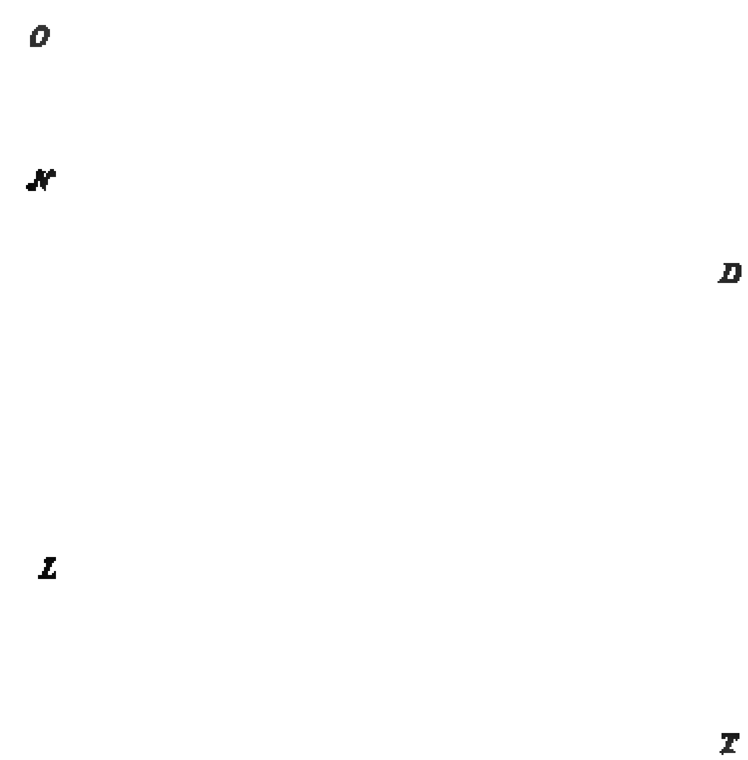


FIG. 109.—BUNDLES OF SMOOTH MUSCLE IN THE DERMA OF THE SKIN OF THE NIPPLE. CHROMIC ACID SPECIMEN.

L, longitudinal, *O*, oblique, *T*, transverse section of a bundle; *D*, derma of the skin; *N*, probably termination of a nerve. Magnified 500 diameters.

face is circular, and the other longitudinal. In the intestinal tract the mucous membrane has two delicate layers (transverse and longitudinal), while the tube possesses in addition two layers, of which the circular is far more developed than the longitudinal. In the stomach, the bladder, and the uterus, numerous oblique bundles run between the circular and longitudinal. In the lower third of the œsophagus smooth

muscles appear, replacing the striped muscles, which are present in the two upper thirds; the boundary line between the two is not sharply marked, as the fibers of both varieties blend with each other (Treitz).

The pregnant uterus is constructed of numerous and large muscle-fibers, also arranged in longitudinal, transverse, and oblique bundles. The bioplasson in this situation is very abundant, giving the spindles a coarsely granular, nearly homogeneous, appearance, without a distinct nucleus. Every large spindle is composed of a number of smaller ones. The boundary line between the latter is often marked at the periphery of the large spindle only, or else a faint oblique trace of demarcation may be observed within a large spindle. (See Fig. 110.)

Blood- and Lymph-vessels are numerous in the smooth muscle-tissue, producing an elongated, more or less rectangular, reticulum. Larger blood- and lymph-vessels are found in the denser formations of connective tissue between groups of bundles, while the delicate perimysium surrounding the bundles contains only capillaries.

The *nerves* of smooth muscle bundles, after repeated plexiform ramifications, branch in the form of delicate axis fibrillæ in the cement-substance between the spindles (M. Löwit). Some observers claim that the axis fibrillæ enter the spindles and terminate in the nucleolus (Frankenhäuser), or pierce the nucleus and the nucleolus, in order to again reach the plexus on the opposite side of the spindle. Here, as well as in striated muscle, a terminal nerve-hill may exist, as indicated in Fig. 109, though its relations are not yet sufficiently studied.

2. Striped Muscle.

Striped muscle is composed of comparatively large fusiform and sometimes blunt spindle-shaped fibers, which are separated from each other by means of a delicate connective-tissue formation, and are held together in bundles by means of broader layers of the same tissue. Each bundle is composed of a varying number of fibers. The fiber is built up by more or less regularly arranged layers of sarcous elements,—formations of bioplasson,—which are interconnected in all directions by delicate filaments of bioplasson, while the meshes between the sarcous elements contain a non-contractile, non-living fluid, which can be artificially pressed out of every muscle.

The distribution of the muscle-fibers in the belly of a mus is best observed in transverse sections, with lower powers of t microscope. (See Fig. 111.)

Each fiber is surrounded, and a certain number of them a inclosed, by fibrous connective tissue, the former being term

T

P

O

C

FIG. 110.—BUNDLES OF SMOOTH MUSCLE OF THE HUMAN UTERUS, SHORTLY AFTER DELIVERY. CHROMIC ACID SPECIMEN.

L, longitudinal, *O*, oblique, *T*, transverse section of bundles: *P*, perimysium, contain blood-vessels, *C*, *E*, plastids in the connective tissue, probably the first trace of muscle-fib Magnified 500 diameters.

internal perimysium, the latter, *external perimysium.* The co nective tissue is the exclusive carrier of blood- and lymph-v sels, also of the nerves, and often contains fat-globules. T

nal perimysium unites into tendinous septa, and these to form the fasciæ and aponeuroses.

ach muscle-fiber, besides, is again inclosed by an extremely ate hyaline, elastic membrane,—the *sarcolemma*,—first deed by Th. Schwann, in 1839. This sheath has not yet been d in the muscle of the heart. The sarcolemma is distinctly

I

F

FIG. 111.—RECTUS MUSCLE OF THE EYEBALL OF MAN. TRANSVERSE SECTION. CHROMIC ACID SPECIMEN.

, external perimysium, containing, besides fat-globules and capillary blood-vessels, artery, *A*, and bundles of medullated nerves, *N*, *PI*, internal perimysium, ensheath- single muscle-fibers, *F*. Magnified 200 diameters.

only in transverse sections of muscle-fibers, but it becomes le also in longitudinal fibers, when broken through, or treatment with dilute acids, which destroy the muscle- e without attacking the sarcolemma. The sarcolemma ars as an apparently structureless, extremely thin, corated membrane, destitute of nuclei. (See Fig. 112.)

The attachment of the muscle-fiber to tendinous or periosteal e is by means of the internal perimysium, while the sarcoma terminates around the blunt or sharp point of the muscle- (C. Toldt). The tendons often exhibit rounded excavations, hich rest the blunt ends of the muscle-fibers; thickened gations of the tendon penetrate to various depths between blunt extremities of the muscle-fibers. The perimysium,

after blending with the tendon or periosteum, is, as a rule, supplied with a large number of plastids. Groups of plastids are sometimes seen filling the triangular space above the point of

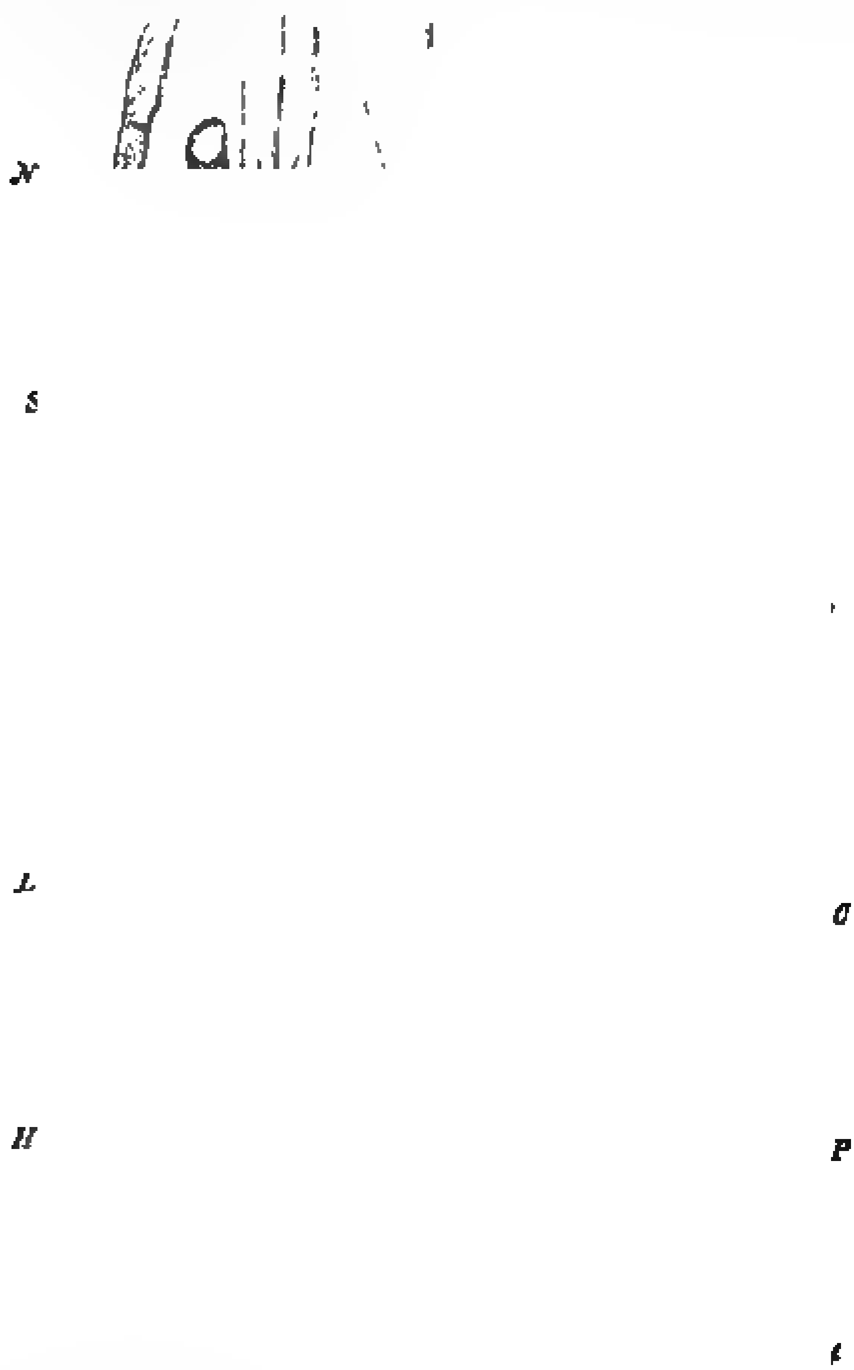


FIG. 112.—MUSCLE OF TONGUE OF MAN. CHROMIC ACID SPECIMEN

L, longitudinal muscle-fiber, broken off and exhibiting its structureless sheath—the colemma, *S*; *N*, medullated nerve-fiber, terminating in the motor hill, *H*; *T*, transverse tion of a muscle-fiber, *P*, the perimysium, holding capillary blood-vessels, *C*, and nerve Magnified 500 diameters.

the muscle-fiber, which often looks as if split into small spind with sarcous elements irregularly distributed. (See Fig. 113.)

Regarding the minute structure of striped muscle-fibers, th is the widest divergence in the views of histologists. Still,

structure is extremely simple, and proved to be so by the description of E. Brücke, in 1857 (see page 127). The only addition I have to make is that all sarcous elements, whatever may be their size and arrangement, are uninterruptedly connected in both longitudinal and transverse directions. The division of the muscle-fiber into the longitudinal fibrillæ of Schwann depends upon a very close aggregation of the sarcous elements in a longitudinal direction. The beaded appearance of these fibrillæ can be explained only by the presence of filaments, connecting the sarcous elements in a lengthwise direction. Muscles kept in alcohol exhibit this characteristic very distinctly. If, on the contrary, sarcous elements are aggregated more closely in transverse direction, either after mechanical injuries, by teasing, or after the application of certain re-agents, such as dilute muriatic, nitric, lactic acid, or the stomachic juice, Bowman's disks will be the result.

The smaller the sarcous elements in a muscle-fiber are, the more rapid and continuous the action of the muscle, and *vice versâ*. The heart, being the most active of all muscles, has the smallest sarcous elements. The slower an animal in its motions, the larger are its sarcous elements. In accordance with what I said on the structure of bioplasson in general, it will be readily understood that contractibility is increased with the smallness of the points of intersection of the reticulum. Normal, fresh muscle-fibers sometimes exhibit very small and irregularly distributed sarcous elements and active contractions under the microscope. Muscles of the crawfish, the lobster, and the water-beetle are, on account of the large size of their sarcous elements, excellent objects for study. As

FIG. 113.—ATTACHMENT OF MUSCLE-FIBERS TO PERIOSTEUM. FROM THE SCAPULA OF A CAT. CHROMIC ACID SPECIMEN.

M, pointed end of muscle-fiber; *S*, the sarcolemma, closely attached to the perimysium, *P*, which blends with the fibrous connective tissue of periosteum Magnified 500 diameters.

Brücke has stated, the arrangement of the sarcous elements in the live muscle-fiber greatly varies; the reasons for this are not yet clearly understood. Nevertheless, the schema of the structure of muscle-fiber was established by Hensen under conditions when the rows of sarcous elements were divided by a single transverse light line, and Merkel divided this line into two. A. Schäfer adopted the schema of two narrow rows between two broad ones. All these conditions are sometimes met with, but they are not by any means the only, or the most common, ones. The theories of Krause's muscle-caskets, and Schäfer's connecting lines, between the two narrow distal rows, have arisen from the erroneous idea that the filaments run *between* the sarcous elements, while in reality they directly connect them, often at their edges. Not infrequently the sarcous elements, under the microscope, appear in oblique position, owing to the general spindle shape of the muscle-fiber, and a dark line is seen on one end of the sarcous element, which is a shortened view of its breadth. This dark line, also, had led observers to wrong conclusions.

Chloride of gold is a good re-agent for bringing to view with great distinctness all the above-described features. That the narrow rows themselves are composed of small, sarcous elements is shown in Fig. 114. This condition is exceptional, and still more so is the appearance of double narrow rows, compared with the appearance illustrated in Fig. 41, page 128.

1

2

FIG. 114.—STRIPED MUSCLE OF THE WATER-BEETLE (HYDROPHILUS PICEUS). STAINED WITH CHLORIDE OF GOLD.

S^1, row of large, and S^2 row of small, sarcous elements, the latter stained deeper violet than the former. All rows interconnected by delicate filaments. Between the rows an uncolored liquid. Magnified 1200 diameters.

That in one muscle-fiber different arrangements of the sarcous elements may occur, can be seen in the muscle of craw-fish. Often in the fresh muscle the regular rows disappear, and a uniform granulation is for a moment visible, while in the next moment the rows are reëstablished. In all these conditions the muscle-fiber executes contractions. (See Fig. 115.)

contraction of a muscle to the naked eye consists in the ing and the broadening of its belly. Accordingly, we see he microscope, in a contracted muscle-fiber, all the rows ous elements approaching each other, and every sarcous becoming broader. This is done at the expense of the ing filaments, which become shortened. The liquid be- he rows spreads by e in the transverse n. By contraction, is lost from and added to the mus- . In extension the fiber is elongated, cordingly the sar- lements gain in and their rows sepa- Ranvier drew atten- the presence of two f muscles even in ls, especially in —the pale trans- and the red opaque s. He claims that e muscles contract apidly, upon appli- f the galvanic cur- an the red ones; pale muscles have marked transverse red a more marked longitudinal striation, and also that clei of the pale muscles are less numerous than those of

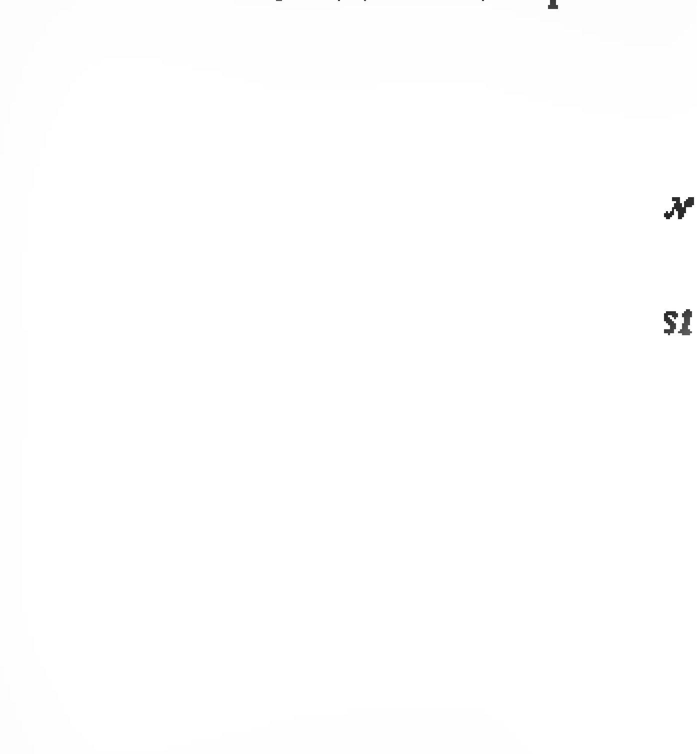


FIG. 115.—STRIPED MUSCLE OF THE CRAW-FISH (ASTACUS FLUVIATILIS). STAINED WITH CHLORIDE OF GOLD.

S^1, row of large sarcous elements, splitting into rows of smaller ones, S^2; between the rows of large sarcous elements rows of small ones; all rows interconnected; N, nuclei on the surface of the fiber. Magnified 1200 diameters.

ransverse sections of muscle-fibers (see Fig. 112) we often central, pale, irregularly granular nucleus, or sometimes h nuclei. Instead of, or in addition to, granular nuclei, we small, irregular, solid lumps of bioplasson in the midst ous elements, which formations correspond to the oblong and to the rows of coarse granules in a longitudinal sec- From the central nucleus radiating offshoots emanate, nterconnect the coarse granules, and group the sarcous s in circular or radiating formations, which are sometimes acefully arranged. These are the celebrated muscle-nuclei

of Max Schultze. They are evidently remnants of the embryonal development, "undifferentiated protoplasm," as M. Schultze himself said. They often fall out, especially from very thin sections, and leave one more central or two more peripheral openings, bounded by a jagged or stellate outline.

The formations termed nuclei really reveal the history of development of the muscle-fiber. *Each fiber is constructed on the plan of a bundle of connective tissue—for example, the tendon. It is likewise composed of one large or a number of smaller territories, and each territory has resulted from the coalescence of a number of plastids, some or portions of which remain unchanged solid or granular bioplasson, while in all surrounding plastids the points of intersection of the bioplasson reticulum assume the regular arrangement of sarcous elements.* At the borders of the territories sometimes a layer of elastic substance is formed, and a whole system of territories is, as a rule, ensheathed by a solidified, so-called elastic substance, the sarcolemma, an offspring of the bioplasson liquid. Th. Margo was the first observer who proved positively that each muscle-fiber arises from a number of plastids, the so-called "sarcoplasts," against the view inaugurated by Schwann, that a single muscle-fiber is an enormously grown "cell."

FIG. 116.—MUSCLE OF THE HEART OF A NEWLY BORN CHILD. LONGITUDINAL SECTION. CHROMIC ACID SPECIMEN.

NN, nuclei on the surface of the muscle-fiber, *CP*, delicate perimysium, with oblong nuclei and capillary blood-vessels. Magnified 500 diameters.

In some places the muscle-fibers have been found bifurcating, f. i., in the tongue, the muscles of the eyeball, and the heart. In the heart the muscle-fibers are very small, freely branching, and united into bundles in the manner of a felt-work. It was said before that here the sarcous elements are extremely small, while the nuclei are very numerous. This is the only muscle which for eighty or more years is in continuous activity — the first to begin and the last to stop. (See Fig. 116.)

The medullated *motor nerves*, upon entering the muscle, split into numerous branches, which course in a transverse or oblique

tion along the fibers; the branches, repeatedly bifurcating ›onnecting, produce a plexus in the perimysium. From this ıs arise the terminal nerve-fibers, each of the muscle-fibers ; supplied with at least one fiber. In some amphibia, the ıllated nerve-fiber penetrates the sarcolemma and divides a number of longitudinal axis fibrillæ on the surface of the le. In most animals has been observed a inal disk, the "motor of Doyère. This is ıely granular discoid, tly elevated formation, ıng with the surface of ıuscle-fiber, with a number f faintly outlined nuclei. medullated nerve-fiber ·aching the hill becomes .ved of its myeline in. nent, while the elastic ine sheath (Schwann's .h) fuses with the sarco. ıa, so that the motor according to the views ost observers, lies un- ·ath the sarcolemma. Krause maintains its ion outside the sarco- ıa (see Fig. 111). Kühne 'ound a broad layer of medullated nerves the hill in all higher als. The axis cylinder ıe nerve-fiber connects tly with the delicate asson reticulum within ıotor hill, and this is . connected by delicate

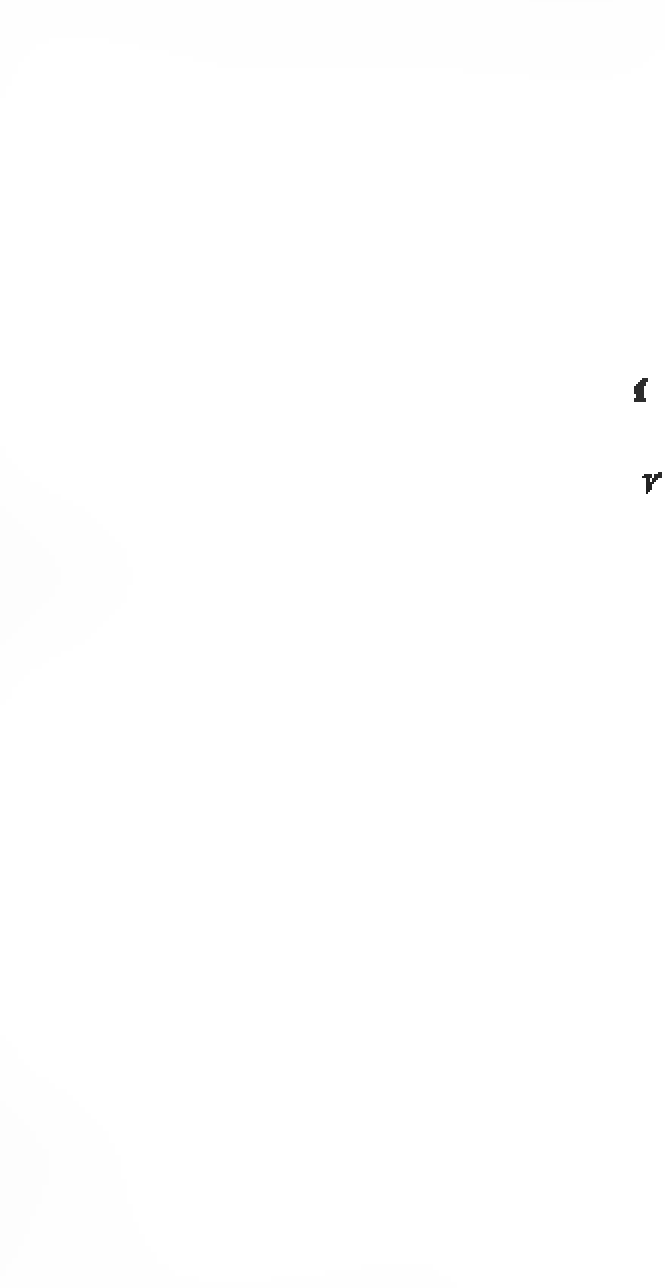


FIG. 117.—STRIPED MUSCLE OF CAT. INJECTED.

A, artery, *V*, vein. Magnified 300 diameters.

·nts to the next sarcous elements. Thus a continuous con- ›n between the nerve and the muscle is established by bridges ing matter. Some medullated and perhaps sensorial nerve- branch in the perimysium without entering the formation ; motor hills.

Blood-vessels are very numerous in striped muscles. They are seen running in the external perimysium as larger arteries and veins, and when reaching the surface of the bundle they ramify into capillaries, which are found in the internal perimysium without entering the muscle-fiber itself. All vascular formations of the striped muscle are characterized by very marked bifurcations at right angles, and this is especially a prominent feature of the branches of the arterioles and the first capillaries arising from them. (See Fig. 117.)

Lymph-vessels are also numerous formations in the tissue of the striped muscle, and, as regular injections show, they always form a closed system of capillaries, which accompany the arterial and venous blood-vessels.

The Structure of the Muscle of the Lobster.

By M. L. Holbrook, M. D.*

When we read the history of those scientific investigations which have been made by our most excellent observers during the last forty years, we can hardly fail to be convinced that even the simplest facts of natural philosophy are only established after long-continued and patient research. Truth is rarely or never reached in a straight line, but only by a tortuous and zigzag course. At times we seem to have it almost within our grasp, and then it becomes lost to view, and we are compelled to seek for it in a new direction. All this is true when applied to the research of muscular structure, as we shall see.

The muscular system, as we know, constitutes the motor apparatus of all complex animal bodies. By it all movement from place to place, all change of shape and form, are accomplished. All motions of the body are based upon the contraction of the two varieties of muscle-fibers, for they possess in the highest degree the same property seen in every portion of living matter, in every simple organism, in every plastid—the power to contract. From this it is fair to conclude that muscle must also be living matter.

Our modern views on the structure of striated muscle date back as far as the year 1839, when Th. Schwann,† in his celebrated researches on the identity of the structure of the animal and plant, maintained that the striated muscle is composed of innumerable, extremely delicate fibrillæ, of a beaded or rosary-like appearance. A number of such fibrillæ, the beads of which stand in one line close together, would, according to his view, form a muscle bundle. If we look at a muscle-fiber, we notice alternating light and dark lines of a definite width, and these, according to Schwann's view, originated in the regularity in which the thick and thin portions of the fibrillæ are placed side by side.

W. Bowman‡ demonstrated that the fibers sometimes break up, when sub-

* Printed from the author's manuscript.

† "Untersuchungen über die Uebereinstimmung," etc. Berlin, 1839.

‡ Todd's Cyclopedia, 1848.

jected to mechanical injuries or chemical re-agents, into transverse disks. The cleavage of the fiber lengthwise gives us the fibrillæ, while a transverse cleavage gives the disks. By splitting the fibers in a longitudinal and transverse direction, this investigator obtained innumerable small cylindrical or square pieces, which he called the *sarcous elements*. He maintained with great positiveness that the striations in the muscle-fiber are due to a difference in the refracting power of the intermediate substance, and that the longitudinal and transverse splitting are not essential properties of the muscle, but are due to mechanical or chemical injuries.

The next investigator who has thrown light on this subject was E. Brücke.* This observer maintains that the sarcous elements are by no means invariable and unchangeable formations in the living muscle, but that they are rows of corpuscles, differently arranged at the moment of death. On examining the fiber with polarized light, he came to the conclusion that the sarcous elements are constructed of very small, invisible particles, which he named *disdiaklasts*. Upon the grouping of these minute bodies, he believed, depended the varying formation of the sarcous elements. Brücke argues that the rows of sarcous elements are double refracting, while the spaces between them are only simple refracting. As to the nature and consistence of these intermediate layers he offers no opinion.

C. Heitzmann † pointed out an interconnection of the sarcous elements, both longitudinally and transversely, by means of delicate filaments of living matter, in the same manner as the granules of bioplasson in the amœba are connected. My own observations point strongly to the correctness of this assertion.

The observations of the investigators now mentioned are the principal sources of our knowledge of striped muscle. The later researches on this subject made by Hensen, W. Krause, W. Engelmann, Heppner, and Alb. Schäfer have added little to our knowledge, as these authors have explained the structure of striped muscle in a complicated manner, and far differently from what we really see. Perhaps Cohnheim's discovery of the peculiar fields in transverse sections of frozen muscle deserve a remark, as they appear to have been formed by the process of freezing, as we shall see later on.

If we take from the lobster a minute piece of perfectly fresh muscular tissue and transfer it, together with a drop of the blood of the animal, to a glass slide, and cover it quickly with a thin cover-glass, we may see, with moderate powers of the microscope, the fibers composing it, of a nearly uniform breadth. These fibers are separated from each other by exceedingly narrow light spaces or rims, which in some places contain a granular mass. A number of fibers are kept together by a delicate fibrous tissue, in which are held the vessels and nerves. These latter features are seen best in a transverse section of the muscle. Within the fiber may be noticed two kinds of substance; one is opaque, of a dim luster; the other is light, uncolored, not shining. In many places the two substances alternate with each other in such a way as to form rows, running in the transverse direction of the fiber, or we may sometimes observe that the opaque substance is distributed without

* "Untersuchungen über den Bau d. Muskelfasern mit Hülfe des polar. Lichtes." Denkschr. d. Wiener Akad. Bd. xv., 1857.

† "Untersuchungen über das Protoplasma." Sitzungsber. d. Wiener Akad. d. Wissensch., 1873.

regularity in the form of granules in the light substance. The rows composed of the bright substance vary greatly in their width. Sometimes a line of it is as broad as the light substance; or the shining substance may very much surpass the light one in breadth; or a broad line may be split in the center by an exceedingly narrow light line. In other words, the bright substance varies greatly in its amount in relation to the light substance.

When we come to use higher powers of the microscope, we find that each shining line is composed of a large number of square, cylindrical, or prism-shaped pieces, which are the *sarcous elements* of Bowman. (See Fig. 118.)

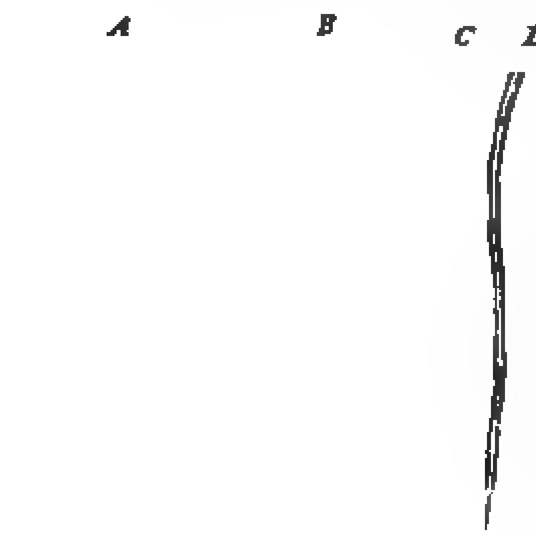


FIG. 118.—MUSCLE OF LOBSTER.

A, muscle-fiber with single rows of sarcous elements, *B*, muscle-fiber with divided rows of sarcous elements; *C*, single torn fibrilla, composed of divided rows of sarcous elements, *D*, single fibrilla without distinct structure. *CD*, features from specimens preserved in chromic acid solution. Magnified 1200 diameters.

We also see that the light layer between the rows of sarcous elements is traversed by extremely delicate grayish filaments, connecting all the rows within a muscle-fiber. When the sarcous elements are separated, so as to render the light interstices between them visible, we again see the grayish filaments connecting the sarcous elements in a transverse direction. Lastly, we see that all the interstices between the muscle-fibers are traversed by delicate grayish threads or spokes, connecting the adjoining muscle-fibers, and also connecting the sarcous elements with the granules present between the fibers.

From this it is evident that the minute structure of the fresh muscle of the lobster is *reticular*. The nodulations of the reticulum correspond to the sarcous elements, and vary greatly in size, while the rectangular connecting fibrillæ always are very delicate.

All observers agree that the sarcous elements are the active agents in muscular contraction, because they are the formations that change their shape and place during the contraction of the muscle, while the intermediate light spaces are filled with a non-contractile liquid.

In order to bring out more perfectly the structure of muscle than could be done in its natural state, I used, with success, a one-half per cent. solution of chloride of gold, which is known to stain living matter violet.

I also tried the freezing of the muscle by means of rhigoline-spray, in order to cut the sections more easily and perfectly. But this changed the texture, at times even completely destroying it, and I was compelled to resort to other means. Here I may state that I suspect the peculiar condition of the muscle discovered by Cohnheim, and previously mentioned, may have been caused by freezing. I did not succeed in obtaining those peculiar fields, described by him, in transverse sections of the muscle of the ox, made while the tissue was slightly frozen.

The next re-agent which I used was a one-half per cent. solution of

chromic acid, which is known to preserve and harden living matter, but not to destroy its character or otherwise injure it. The results with the chromic acid specimens were found to be the same as those observed in the fresh muscle. Here, too, the alternating layers of sarcous elements and the interstitial layers were plainly recognized. The rows of sarcous elements varied greatly in breadth and form. If we tease a chromic acid specimen, we obtain delicate longitudinal fibrillæ, because we break the transverse connections—the filaments of living matter which unite them together. Such an artificially isolated fibrilla may appear beaded, as was asserted by Th. Schwann, or it may exhibit a nearly uniform width throughout its entire length, or the entire fibrilla may appear bright and homogeneous, and show no trace of any difference in its optical properties in any part. This can be explained by the fact that the sarcous elements within the muscle-fiber may coalesce, or approach each other so closely that the intermediate light substance becomes invisible. We may explain the beaded condition of the fibrilla either by saying that the living matter produces a solid square piece, —the sarcous element,—which above and below is hollowed out and incloses the interstitial liquid, or by saying that from both edges of the sarcous element connecting filaments run to the neighboring sarcous element.

In a longitudinal section of a muscle-fiber, we not infrequently meet with oblong solid masses of a highly refracting nature, which are termed by the authors, the nuclei. That such formations are present, not only on the surface of the muscle-fiber, but also in its interior, is best demonstrated in transverse sections, where, in the center of the fiber, we almost invariably observe a more solid mass, with stellate offshoots which subdivide the muscle-fiber into smaller fields. The presence of these large bioplasson masses within the muscle-fiber has a close connection with the history of the development of the muscle. Similar formations do, however, occur in the muscles of mammals. I have especially observed globular or oblong bioplasson masses in the center of the muscle-fiber of the ox. In making transverse sections, these masses are very liable to fall out, or, perhaps, be drawn out by the razor, leaving an empty space behind. This gives the incorrect impression that the muscle-fiber is hollow in its center.

Every muscle-fiber in mammals is known to be ensheathed in an extremely delicate, firm, so-called elastic or hyaline membrane—the *sarcolemma*. This layer is present around the muscle-fibers of the lobster also.

The statement of E. Brücke, which has gained general assent, that the sarcous elements are possessed of a double refracting power, is, I am convinced, incorrect; at least, my own observations on the muscle of the lobster with polarized light are not in accord with this view. I made a large number of observations on specimens prepared in different ways, and also with perfectly fresh specimens, moistened with a drop of the blood of the animal, and could only obtain the phenomena of polarization in specimens of some thickness. In every case when the specimen was very thin, and allowed the light to pass through it freely, there was no evidence of polarization. W. Kühne (1864) failed to obtain polarization with the amœba, and my observation with the muscle-fiber of the lobster coincides with his.

It is Doyère's and Kühne's discovery that the motor nerves, which control the action of the muscles, never enter the muscle fibers, but terminate on their surface, generally in the form of hills, the so-called *motor hills*. I have observed similar formations in the muscle of the lobster, and, further, I have

observed a direct connection of the bioplasson of the motor hill with the adjacent sarcous elements by many delicate grayish filaments of bioplasson Thus, it becomes intelligible that the influence of the motor nerve may be transmitted to a number of sarcous elements, from which it may spread toward the points of the fiber and produce contraction.

As a result of these investigations, I am led to the conclusion that the striated muscle of the lobster is constructed on the same plan as the striated muscles of the highly developed mammals. It is a formation of living matter of a reticular structure, the points of intersection being the sarcous elements, the means of connection being delicate filaments extending in a longitudinal and transverse direction.

IX.

NERVE-TISSUE.*

NERVE-TISSUE is composed of living matter, seen either as an extremely delicate reticulum, or as apparently homogeneous filaments—the axis-cylinders. The reticulum is of a uniform width, without well-marked points of intersection (see page 128, Figs. 42 and 43), as seen in the gray substance of the brain and the spinal cord. In the reticular bioplasson, formations are imbedded, which bear resemblance to nuclei, with distinct walls and larger branching bodies, usually nucleated and reticular in structure—viz.: the ganglionic elements. From the reticulum of the gray substance, and also from that of ganglionic elements, somewhat thicker filaments emanate,—the axis-cylinders,—which are the essential part of the structure of nerves. The axis-cylinders, as a continuous formation, pervade all tissues of the body except the horny epidermal tissue, and serve for the transmission of either sensory impressions from the periphery to the center, or motor impulses from the center to the periphery.

Nerve-tissue, as such, is destitute of blood- and lymph-vessels.

* This chapter will be found more deficient in histological facts than, perhaps, any other of the book. The reason is that I have not as yet given very much time to the study of nerve-tissue, this being the most unsatisfactory and discouraging portion of histology. I prefer, therefore, to be incomplete in this matter until I am able to make positive assertions, based on personal observation, instead of relying too much on what others have said. The particulars that I shall give concerning the architecture of the brain I have taken from the ingenious publications of Th. Meynert.

It is only the accompanying and ensheathing connective tissue which carries vessels.

In order to facilitate the study of the nervous system, it is convenient to subdivide it into three main portions, all of which form one continuous mass of tissue—*i. e.*, the central portion, the conducting portion, and the terminal portion.

1. Nerve-centers.

In the brain and the spinal cord, it is only the gray substance which can be called nerve-center, as the white substance is composed of conducting nerves. The ganglia of the sympathetic nerves may also be considered as central organs.

(A) Brain. According to Th. Meynert,* the gray substance of the brain may be divided into four groups:

(a) The uppermost mass of gray matter, from which the entire white substance of the brain takes its rise, is *the superficial gray substance of the cerebral lobes—the cortex cerebri;*

(b) Collections of gray matter are the *ganglia of the cerebrum*—the corpus striatum, the three members of the lenticular nucleus, the thalamus opticus, and the corpora quadrigemina;

(c) The *tubular gray matter*, which invests the cavities of the brain as a direct prolongation of the gray substance of the spinal cord, traceable through the fossa rhomboidalis, the aqueduct, the middle ventricle, into the tuber cinereum and the infundibulum;

(d) The *gray substance of the cerebellum*, arranged partly in layers, partly in central aggregations, and in connection with the gray formations of the caudex cerebri, which are traversed by the medullary substance of the cerebellum.

The gray masses are connected by means of fibrous tracts of the white substance. The gray cortex of the brain receives all the sensory impressions from the outer world, and from it arise the motor impulses, communicated to the motor nerves.

The medullary or white substance of the large hemispheres of the brain—the corona radiata—furnishes the routes of this *system of projections of the first order*; and, moreover, this system is connected by bundles of nerve-fibers with the cerebellum. The fibers of this projection system take mostly a radiating course; additional formations of this system are the commissures in the corpus callosum, which connect the corresponding portions of the right and the left side, and the systems of association, which connect different regions of the cortex in one hemisphere.

The ganglia of the cerebrum interrupt the projection system of the first order, and in them a reduction of the number of the fibers of this system

* "A Manual of Histology," by S. Stricker. American edition, 1872.

takes place. The bundles of nerve-fibers, leaving the ganglia and entering the central tubular gray investment of the brain, are considered as the *projection system of the second order.* This system is composed of two portions. One for the impulse of voluntary muscle action, arises from the corpus striatum and the nucleus lenticularis, penetrating the *pedunculus* cruris cerebri; the other portion is the route of reflex motion, and takes its origin from the thalamus opticus, the corpora quadrigemina, and the corp. geniculatum internum, running into the *tegmentum* cruris cerebri.

The tubular gray matter gives rise to the peripheral nerves, which are greatly increased in number, as compared with their reduction in the ganglia. The peripheral nerves represent the *projection system of the third order.* The accumulations of nerve elements in the tubular gray matter are termed its nuclei, and this gray matter itself lies bare on the base of the brain in the lamina perforata posterior and the infundibulum.

The cerebellum is independent, to a certain degree, of the projection systems of the brain, though connected by the crura cerebelli with the cortex cerebri, and probably by the crura cerebelli ad pontem. It connects with the spinal cord through the fasciculi gracilis and cuneiformis and the restiform bodies.

The *medulla oblongata* connects the brain with the spinal cord; in this formation the projection system of the second order is reduced to its simplest form, as observed in the spinal cord. Both halves of the medulla oblongata are connected by the pyramidal decussations, and both contain a number of gray nuclei, the superior and inferior olivary bodies and the nucleus of the pyramis.

The *cortex of the brain* has a common form of stratification, from which, however, deviations are found in the occipital extremity, in the cortex bounding the fossa Sylvii, in Ammon's horn, and in the olfactory bulb.

There are five strata of the cortex cerebri in man, which are as follows:

(a) The most superficial layer, which consists mostly of connective tissue, and of a few small ganglionic elements and delicate nerve-fibrillæ;

(b) The second layer is marked by a large number of small, multipolar ganglionic elements;

(c) The third and broadest layer contains multipolar ganglionic elements, decidedly surpassing in size those of the second layer. Their shape is either pyramidal or fusiform, with the longitudinal direction vertical to the brain surface. Their upper projection divides into a delicate reticulum; the lower passes without division toward the white substance;

(d) The fourth layer contains small globules, with very delicate offshoots: these, possibly, may be only connected with the sensory nerves;

(e) The fifth layer holds spindle-shaped ganglionic elements, which lie parallel to the surface of the brain, and have undivided offshoots. Meynert considers them to be the intercalated cells of the system of association.

In the occipital extremity there are eight layers; the third typical layer is wanting, but the granular formation is composed of three layers. In the cortex, bounding the fossa Sylvii, the fifth layer is markedly developed, producing the claustrum. The cortex of the Ammon's horn has no granular layer, while the motor elements of the second and third typical layers are very abundant. The cortex of the olfactory bulb in its upper portion is covered with a white layer, and exhibits from below upward: a layer of non-medullated nerve-fibers, a layer of the glomeruli olfactorii, a layer of

spindle-shaped ganglionic elements, and a layer of granules, the fibers between which unite with those of the uppermost white medullary layer.

The Origin of the Cerebral Nerves. As before stated, the tubular gray matter, which is located around the aquæductus Sylvii and extends backward, connecting with the floor of the fourth ventricle, gives rise to the cerebral nerves. In this gray matter we find groups of multipolar ganglionic elements, which are known to be the nuclei of the nerves. There are also exceptional formations found in the tracts along the anterior pair of the corpora quadrigemina, which consist of very large globular ganglionic elements. These constitute the sensitive roots of the trigeminus. Similar formations are found in the anterior nucleus of the root of the auditory nerve. Brown and black pigment granules are present in the substantia ferruginea of the fossa rhomboidalis and in the substantia nigra of the pedunculus cerebri. The nucleus of the hypoglossal nerve has very large ganglionic elements and a reticular formation, produced by a close combination of layers of the gray and white substance. In the medulla oblongata such formations occur: in the pyramis, in the fasciculi restiformis, gracilis, and cuneiformis.

The *olfactory nerve* arises from the olfactory bulb; its external and larger tract is connected with the gyrus uncinatus or subiculum cornu Ammonis; its internal tract connects with the frontal extremity of the gyrus fornicatus, and its middle tract with the head of the corpus striatum.

The *optic nerve* very probably starts from several nuclei, one of which is, perhaps, the anterior pair of the corpora quadrigemina (Corp. bigem. super.).

The *motor oculi and trochlear nerve* spring from a cylindrical group of elements below the aquæductus Sylvii, near the median line. This nucleus, by means of nerve-bundles, is in connection with the corpus striatum and the corpus bigem. superius.

The *trigeminus nerve* has several nuclei. The upper sensitive nucleus is composed of groups of ganglionic elements along the tegmentum of the anterior pair of the corpora quadrigemina; the middle sensitive nucleus is located below the upper one; the under sensitive nucleus exists in the medulla oblongata, and is traceable into the posterior column of the spinal cord. The motor root of this nerve has its nucleus in the fossa rhomboidalis, extending anteriorly to the aquæductus Sylvii.

The *abducent nerve* originates from a nucleus in the anterior portion of the fossa rhomboidalis, and is in connection with the deeper situated nucleus of the facial nerve.

The *facial nerve* originates from three roots arising from a nucleus in the depths of the floor of the fourth ventricle, where large ganglionic elements with bulky offshoots are seen.

The *auditory nerve* has its nucleus in the floor of the fossa rhomboidalis, extending from the median line toward the pedunculi cerebelli, and gaining in thickness as it advances. The median portion is the inner acoustic nucleus, which may be divided into three parts. The broad outer portion has large pyramidal ganglionic elements. An anterior nucleus is located at the side of the pedunculus cerebelli.

The *glosso-pharyngeal and vagus nerve* arise from one common nucleus, the anterior portion of which, reaching the internal acoustic nucleus, belongs to the glosso-pharyngeal nerve, while the posterior portion, in the ala cinerea of the fossa rhomboidalis, constitutes the vagus.

The *spinal accessory nerve* originates partly from the nucleus of the vagus,

partly from a columnar formation, closely connected with the nucleus of the vagus and traceable into the anterior column of the spinal cord.

The *hypoglossal nerve* has its nucleus in the posterior portion of the fossa rhomboidalis, close to the median line. There is also a direct passage of fibers from the crus cerebri into the hypoglossus by way of the raphe.

(B) Gray Substance. The gray substance is the only nerve-tissue found in the brain of the lower vertebrates. Here, instead of ganglionic elements, nuclei are present, which, especially around the ventricles, collect in regular rows, representing in its simplest relations the bioplasson of the nervous center. (See Fig. 118.)

The presence of connective tissue in the gray substance is unquestionable, as it is the carrier of the numerous blood-vessels of the gray substance. The finest ramifications of connective tissue, however, have not been discovered, but are still the subject of animated controversy among histologists. It seems that the finest offshoots of the ganglionic elements, producing an extremely delicate reticulum, first discovered by *T. Gerlach*, deserve to be classified among nervous structures, inasmuch as in this reticulum there is no indication of a basis-substance—an essential part of all varieties of connective tissue. It may be that connective and nervous tissue blend with each other so intimately that an accurate determination of either of them is impossible.

The blood-vessels of the gray substance are characterized by the presence of a lymph-sheath. His was the first to draw attention to this fact. According to him, each blood-vessel is ensheathed by an adventitial coat of endothelial structure, and the space between the tube of the blood-vessel and the investing tube of the lymph-vessel varies greatly in width. Boll's view concerning the lymph-sheath is somewhat different.

The *cortex of the cerebellum* is composed of three layers. The outermost is called the *gray layer*, and exhibits, with low powers of the microscope, a delicate granular appearance, which, with high powers, proves to be a reticulum, considered by histologists to be a connective-tissue formation. Within the reticulum there are scanty, small, branching ganglionic elements; on the innermost portion we notice fibrous tracts, in a direction parallel to the surface. The middle so-called *cell-layer* contains large, branching, and nucleated ganglionic elements, mostly pear-shaped, standing in a vertical or oblique direction to the surface. These bodies, in honor of their discoverer, are termed Purkinje's cells. From the outer pole of each corpuscle originates an offshoot,

which freely bifurcates and sends its branches into the outer gray layer. .From the inner pole arises an offshoot, which, without ramifications, traverses the granular layer and runs into the

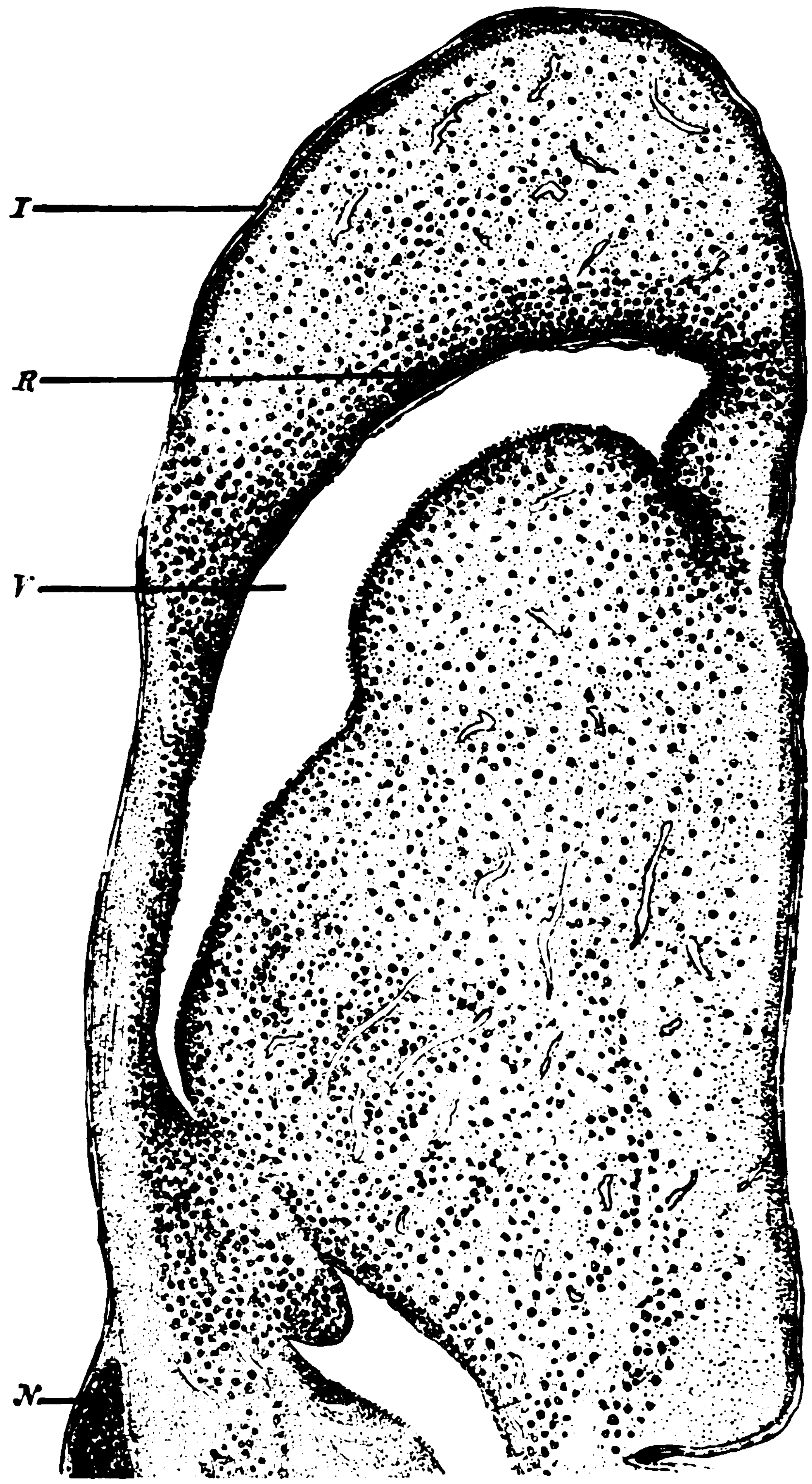


FIG. 118.—ANTERIOR LOBE OF THE BRAIN OF A TREE-FROG. SAGITTAL SECTION.

I, investing sheath of connective tissue; *R*, rows of nuclei; *V*, ventricle, with endothelial investment; *N*, bundle of medullated nerve-fibers. Magnified 50 diameters.

white substance. The inner so-called *granular layer* is composed of heaps of small globular bodies, mostly of a high degree of

refraction and similar to the bodies found in the granular layers of the retina. Their nature is unknown.

The *hypophysis cerebri* exhibits two lobules, which are separated from each other by a number of venous blood-vessels. The posterior small portion is an elongation of the infundibulum, and probably belongs to the nervous structures. The anterior large lobule is a glandular formation, and, as Von Mihalkovits has demonstrated, was originally a club-like prolongation of the oral cavity of the embryo.

The *pineal gland* is attached to the brain by means of connective tissue, and has no nerve elements in its interior. It is composed of alveoli, containing corpuscles in a reticular arrangement. In the middle portions, the alveoli are filled with the *cerebral sand*, consisting of globular or mulberry-like concretions, as a rule exhibiting a concentric striation.

The organic material in these bodies is infiltrated with carbonate of lime and phosphate of magnesia.

The *gray substance of the spinal cord* is in the center throughout the whole length of the cord, reaching the greatest size in the cervical and the lumbar portion, where the largest nerves for the extremities arise. The general form of the gray substance in tranverse section resembles a butterfly, the two anterior larger wings being distinguished from the posterior smaller ones by a shallow depression. Each half of the gray substance represents a column, and the two are connected by commissures traversing the so-called medullary cone or commissure leaf (Markblatt, Commissurenblatt). (See Fig. 119.)

Each gray column exhibits a large *anterior*, or *motor*, horn, and a smaller *posterior*, or *sensitive*, horn. In the outer portion of the anterior horn we find very large motor ganglionic elements, varying greatly in size and shape in different portions of the spinal cord. In some portions of the posterior horn ganglionic elements are absent, and in their place accumulations of nuclei-like bodies are observed. The posterior horn, from its soft consistence, bears the unnecessary name, "gelatinous substance," which name by some histologists is given to the commissural portions in the neighborhood of the central canal. The latter portion is also called the central ependyma thread, or the central gray nucleus. The central canal, a prolongation of the cerebral ventricles, is lined by a columnar endothelium, which in youth shows distinct cilia, while in older individuals the cilia are not so plainly marked.

(C) Ganglionic Elements. The *ganglionic nerve elements* ("ganglion cells") are scattered throughout the gray substance of the

brain and spinal cord; they vary greatly in size and shape. The smallest of these bodies are kindred to those formations of the gray substance considered as nuclei. Many of them are doubtful in their nature—f. i., the "cells of Deiters," which by some observers are considered as nervous, by others as connective-tissue, corpuscles. The larger ganglionic bodies exhibit a distinct angular or fusiform shape, and give rise to nerve-fibers, therefore are real nerve-centers. The largest ganglionic elements are found in the lateral portion of the anterior or motor horn of the spinal cord.

In the spinal cord, the groups of ganglionic elements are dis-

FIG. 119.—SPINAL CORD OF FROG. TRANSVERSE SECTION.

AF, anterior longitudinal fissure; *PF*, posterior longitudinal fissure, *W*, white substance; *AC*, anterior commissure of the gray substance; *MG*, anterior or motor horn of the gray column, rich with ganglionic elements, *SC*, posterior or sensitive horn; *CC*, central canal; *PC*, commissure layer, with fibers of the posterior commissure, *MR*, anterior or motor roots; *PR*, posterior or sensitive roots of nerves; *MN*, intervertebral ganglion, the connection with *PR* broken; *V*, pia mater, holding a blood-vessel. Magnified 50 diameters.

tributed in the following way: In the anterior horn we notice three groups of ganglionic elements, not distinctly marked throughout the whole; the largest group lies in the lateral portion; a smaller group in the anterior portion, near the greatest protrusion of the anterior horn, and a third group, the smallest,

near the median line. A fourth group of ganglionic elements, constituting the *columns of Clarke*, is found only in the thoracic portion of the spinal cord, in the foremost part of the posterior horn, near the posterior commissure. In the posterior horn the ganglionic elements are always small, scattered, and with comparatively few offshoots. The illustration is taken from the third group of the anterior horn. (See Fig. 120.)

The ganglionic elements are bioplasson formations, which, according to the number of offshoots, are termed unipolar,

FIG. 120.—GANGLIONIC ELEMENTS FROM THE ANTERIOR OR MOTOR HORN OF THE SPINAL CORD OF A CHILD.

U, unipolar, *B*, bipolar, *T*, tripolar, *Q*, quadripolar ganglionic element, *G*, gray substance, containing small, shining nuclei, and a number of axis-cylinders; *CL*, capillary blood-vessel, longitudinally, *CT*, capillary blood-vessel, transversely, cut, each surrounded by the lymph-sheath. Magnified 800 diameters.

bipolar, tripolar, quadripolar, or multipolar. The number of offshoots is in close relation with the size of the corpuscle. A light space is often found around the ganglionic element; this is the so-called "periganglionic space," which, in all probability, is artificially produced by the shrinkage of the neighboring tissue.

The reticular structure of these bodies was first described by C. Frommann, in 1867. This reticulum is usually very distinct, especially when the formations of nuclei, nucleoli, and nucleolini (L. Mauthner) are well marked. The reticular structure is not peculiar to these bodies, but is one of the general features of all bioplasson. The offshoots of the ganglionic elements are of two kinds: the broad, so-called *protoplasmic offshoots of Deiters*, and the narrow, *axis-cylinder offshoots*. Of the former, we know that they connect neighboring elements and branch out into the gray substance, where they divide into an extremely delicate reticulum, first described by T. Gerlach. This author further asserts that the ganglionic elements of Clarke's columns, and perhaps those of the posterior horns also, have no other than branching offshoots. The narrow axis-cylinder offshoot takes a more or less straight course, and enters the white substance without ramifications, thus being a future nerve-fiber. Axis-cylinder offshoots arise also from the gray substance, without any connection with ganglionic elements.

M. Schultze and others maintain that the axis-cylinder has a delicate fibrillated structure, and that the fibrillæ spread in the body of the ganglionic element after the manner of a fan. This assertion is based upon observation of teased specimens, and should be cautiously received. I have often studied the brain structure of freshly killed rabbits, both with and without the addition of an indifferent liquid, and could never discover any fibrillated structure in the axis-cylinders. Both the broad axis-cylinders and the broad offshoots have a delicate reticular structure, like that seen in the ganglionic elements themselves. The finest axis-cylinders are apparently solid or slightly vacuoled. In the gray substance, especially in young animals, many axis-cylinders exhibit varicose enlargements, which are considered by histologists to be post-mortem appearances. This, again, is an assertion which I must contradict, as I have frequently observed such enlargements in fresh specimens (see page 129, Fig. 43). I must also contradict the assertion of histologists that medullated nerve-fibers arise directly from ganglionic elements. These bodies are present only in the gray matter, where no medullated nerve-fibers exist, but only bare axis-cylinders; obviously, therefore, the axis-cylinder, emanating from the ganglionic body, must run for a certain distance without a myeline investment.

Very little is known regarding the course taken by the nerve-

ers within the gray substance of the spinal cord. The nerves the anterior or motor roots originate from the motor ganglia;

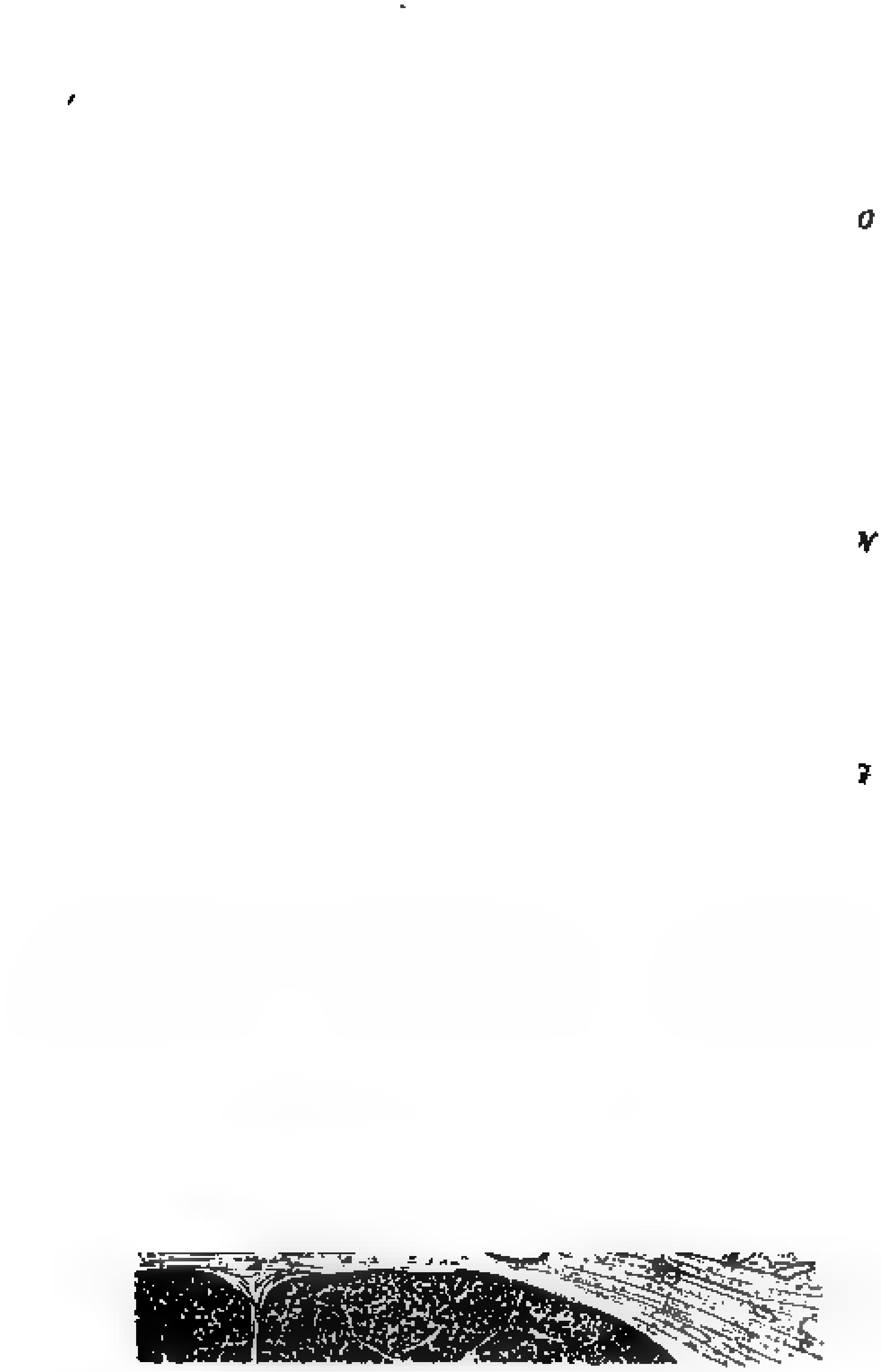


FIG. 121.—ANTERIOR PORTION OF THE SPINAL CORD OF A CHILD. TRANSVERSE SECTION.

anterior longitudinal fissure, *P*, pia mater, *W*, white substance, traversed by offshoots e pia mater, *O*, passage of the anterior or motor nerves through the white substance; *G*, substance, containing *N*, ganglionic elements, *C*, central canal, containing granular ulated cerebro-spinal liquid. Magnified 150 diameters.

small number of nerve-fibers reach the motor roots from the hite substance. From the reticulum of Gerlach nerve-fibers

arise which reach the opposite horns, partly through the anterior commissure, partly by running upward to the medulla oblongata, where they decussate. The posterior roots also arise from two bundles, one of which traverses the posterior commissure. According to Gerlach, it is also probable that from the reticulum of the posterior horn nerve-fibers originate, which in this horn and in the white substance take a centripetal course. The structure of the posterior horn is considered to be mainly connective tissue, especially in its gelatinous portion.

(D) The *white substance of the spinal cord*, as well as that of the cerebrum and cerebellum, is composed of medullated nerve-fibers, which in the spinal cord run in a longitudinal direction and furnish the outer investment with its nerve supply. This substance borders on the anterior and posterior longitudinal fissure, and is pierced by numerous offshoots of the pia mater, which divide and subdivide the nerve-bundles into larger and smaller groups. (See Fig. 121.)

The anterior and posterior roots of the spinal nerves also produce smaller fissures in the lateral portions of the white substance, the sulcus lateralis anterior and posterior, by which the white substance is divided on either side into an anterior, a lateral, and a posterior cord. In the thoracic and cervical portions of the spinal cord the posterior part is again divided into halves, the middle division of which is termed the delicate cord, and the larger lateral portions the wedge-shaped cords.

The medullated nerve-fibers of the white substance vary greatly in size. The coarser offshoots of the pia mater send lateral prolongations between the nerve-fibers, every one of which has a delicate investment of connective tissue—the perineurium internum or neuroglia. According to Gerlach, this connective tissue is rich in elastic substance, and furnished with small globular or angular nuclei, but has a relatively scanty supply of blood-vessels.

In transverse sections of the white substance, we especially recognize the medullated nerve-fibers by their graceful ensheathing reticulum of connective tissue and their central, bright axis-cylinder, which readily takes up the carmine stain. (See Fig. 122.)

Each nerve-fiber is provided with a delicate outer investing membrane—the *myeline sheath*, or Schwann's sheath—which holds flat, oblong (in the transverse section spindle-shaped) nuclei. Former observers denied the existence of this sheath;

but Gerlach concluded that it must be present, and I positively maintain its existence. The next layer is the *myeline investment*, which, in thin sections, is invariably destroyed. In its place, a delicate, knotty reticulum is visible, to the existence of which Kühne and Ewald* first drew attention. These observers claim that the reticulum in the myeline layer is horny or keratoid, because it resists digestion with pepsine and tripsine. They also traced in the gray substance a similarly resistant reticulum. In the meshes of this reticulum the myeline is contained. The myeline investment in some nerves is very narrow, and in others completely wanting. The next layer is a delicate sheath—the

PE

PI

M

A

FIG. 122.—WHITE SUBSTANCE OF THE SPINAL CORD OF A CHILD. TRANSVERSE SECTION.

PE, connective-tissue offshoot of the pia mater—the external perineurium; *PI*, lateral connective-tissue offshoots around the nerve-fibers—the internal perineurium, *M*, oozed-out myeline investment, with inclosing myeline sheath, *A*, axis-cylinder, with inclosing axis-cylinder sheath. Magnified 600 diameters.

axis-cylinder sheath, discovered by L. Mauthner—similar to the myeline sheath. The center is occupied by the bright, homogeneous-looking, usually roundish axis-cylinder, from which delicate radiating spokes emanate and go to the axis-cylinder sheath.

In longitudinal sections the axis-cylinder is plainly visible only where the investing sheaths are stripped off, but where the

* Verhandlungen der Heidelberger Gesellschaft, 1876.

sheaths are preserved and the myeline is absent, a faint trace only of the axis-cylinder is discerned. We recognize the myeline sheath with its oblong nuclei; at pretty regular intervals it sends out transverse septa through the myeline investment, the significance of which will be spoken of later. The reticulum of the myeline sheath is very distinct where the myeline has oozed out. The axis-cylinder sheath can be recognized here and there, though it is often very difficult to distinguish it from the stretched myeline sheath, which may lie close to the axis-cylinder. (See Fig. 123.)

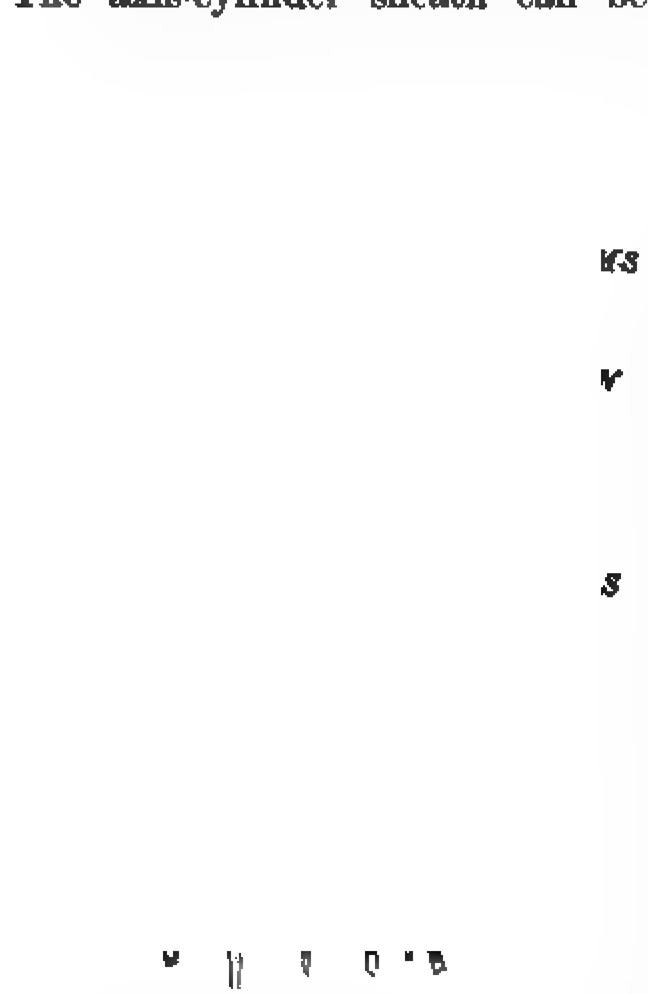


FIG. 123.—WHITE SUBSTANCE OF THE SPINAL CORD OF THE HORSE. LONGITUDINAL SECTION.

A, axis-cylinder, *AS*, axis-cylinder sheath, *N*, nucleus of the myeline sheath, *MS*, myeline sheath, with oblong nuclei. Magnified 600 diameters.

(E) The Connective-tissue Investments of the Brain and the Spinal Cord. The brain and spinal cord have three membraneous investments — the dura mater, the arachnoidea, and the pia mater. The spaces between these are filled with a varying amount of cerebro-spinal liquid. The space between the dura mater and the arachnoid is called the *subdural space;* that between the arachnoid and the pia mater bears the name *subarachnoidal space*, and is traversed by trabeculæ of connective tissue, uniting the membranes. In the spinal canal this space is subdivided into halves by the Lig. denticulatum, and contains the large blood-vessels at the base of the brain. A third space between the pia mater and the surface of the brain may be produced artificially by the injection of liquids from without; it is called the *epicerebral space.*

The *dura mater* of the skull represents the periosteum of the cranial bones, while in the spinal canal there is a periosteal investment of the vertebræ, in addition to the dura mater. It is composed of very firm, dense interlacing fibers of connective tissue. Its outer layer is well provided with blood-vessels enter-

ing the skull-bones; while the inner layer, that which alone forms the dura mater of the spinal cord, has a comparatively scanty supply of blood-vessels. The inner surface of this membrane is lined with a delicate layer of endothelia.

The *arachnoidea* is composed of much more delicate bundles of connective tissue than the dura mater (see Fig. 55, page 160), and probably contains neither blood-vessels nor nerves. Both its surfaces are covered with endothelia. It sends numerous trabeculæ in an oblique direction into:

The *pia mater*, which is also constructed of delicate interlacing bundles of connective tissue and supplied with numerous blood- and lymph-vessels and nerves. The prolongations of the pia mater into the brain and spinal cord convey mainly capillary blood-vessels, as the division of the arteries into capillaries takes place before their entrance into the nerve-centers. The telæ choroideæ are freely vascularized formations of the pia mater; their blood-vessels are coiled in bundles, and produce the lobules which are covered with large, partially ciliated, endothelia, often containing pigment and fat-granules.

(F) The Ganglia. Nerves of the cerebro-spinal system are provided in certain localities with spindle-shaped, or globular or crescent-like, enlargements, the ganglia, which consist of an accumulation of ganglionic elements, greatly varying in size, and arranged either in rows or in clusters, which are more numerous at the periphery of the ganglion than at its center. The manner in which nerve-fibers are connected with the ganglionic elements has not yet been elucidated. Each ganglion is ensheathed by a connective-tissue capsule, and divided by septa of connective tissue into smaller portions; sometimes every single large ganglionic element is inclosed by a connective-tissue sheath, the connective tissue being always freely supplied with blood-vessels.

The ganglia of the sympathetic nerve system contain smaller ganglionic elements and numerous globular bodies, exhibiting the features of lymph-corpuscles or nuclei rather than those of ganglionic elements. The ganglionic bodies are, as a rule, multipolar. In those of the frog the central axis-cylinder was found to be surrounded by a delicate spiral fiber (Beale), which is also considered to be an offshoot of the ganglionic element. J. Arnold claims that the straight central fiber comes from the nucleolus of the ganglionic body, while the spiral fiber originates from its periphery. All these assertions have been contradicted, and need further proof before they can be received.

2. Nerves.

Nerves are thread-like formations of bioplasson connecting the nerve-centers with the periphery of the body. They are of two kinds: first, those endowed with a myeline investment,

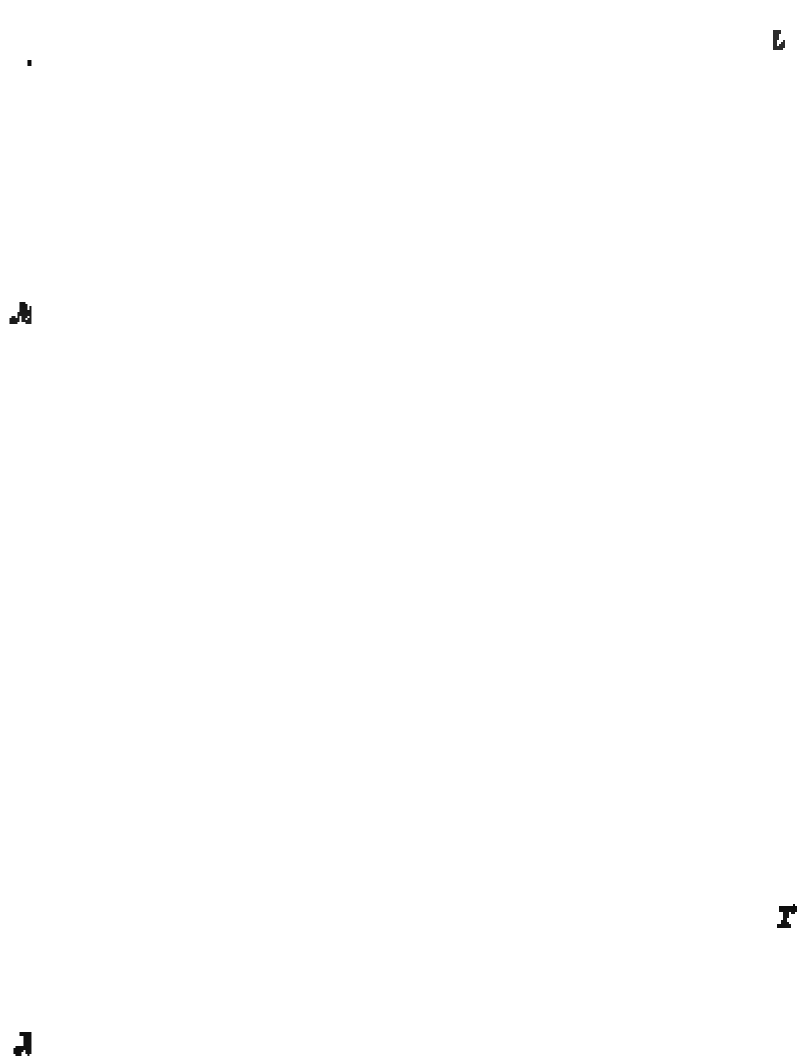


Fig. 124.—Branch of the Motor Oculi Nerve of Man.

L, longitudinal, *T*, transverse section of the bundle, *PE*, external perineurium; *PI*, internal perineurium; *ML*, myeline investment; *A*, axis-cylinder, *M*, transverse sections of muscle-fibers. Magnified 600 diameters.

the medullated or white nerves; and secondly, those which are without a myeline investment, the non-medullated or gray nerves.

(a) Medullated Nerves. These compose the white substance of the brain and of the spinal cord, and all the nerves springing from the brain and the spinal cord, with the exception of the olfactory and auditory nerves. They invariably run their whole course without branching. The constituent parts of medullated nerves are best studied in specimens where, owing to a wavy course of the nerves, the razor in cutting produces alternately longitudinal and transverse sections. (See Fig. 124.)

We see that each nerve-bundle is made up of a varying number of fibers. The bundle is surrounded by a somewhat broader layer of fibrous connective tissue, the *external perineurium*, from which arise delicate membranes of connective tissue, ensheathing each single fiber; this formation has received the name of the *internal perineurium.* Both the external and internal perineurium are provided with a large number of blood-vessels. Next, there is a delicate hyaline layer with distinct nuclei, the *myeline sheath*, or sheath of Schwann. This sheath incloses a layer of a semi-fluid fatty substance, the *myeline* or *nerve-fat*, or the white substance of Schwann. At comparatively regular intervals the myeline investment is traversed, according to L. Ranvier, by transverse septa, which he found to be in connection with the axis-cylinder sheath (Mauthner), and closely related to the development of the medullated nerves. The myeline investment is separated from the central axis-cylinder by a delicate hyaline sheath, the *axis-cylinder sheath* (Mauthner). This incloses the central *axis-cylinder*, which may be either round or oblong, and is the conducting part of the nerve-fiber. In transverse sections this is easily recognized from its bright, almost homogeneous, appearance, while in longitudinal sections it is invisible if the myeline be present, and only faintly visible if the myeline be absent. Not infrequently we find two axis-cylinders in one nerve-fiber. Together with the large medullated nerve-fibers in the same bundles there are sometimes found fibers without and also fibers with a very delicate myeline investment. The latter formations probably belong to the sympathetic system.

The myeline is a fatty substance, differing from ordinary fat, however, in both its optical and chemical characteristics. From the fact that a delicate reticulum is still preserved in the space between the sheaths of the myeline and that of the axis-cylinder (see Fig. 123), and from the fact that fat is a product of living matter, we may conclude that the myeline is, perhaps, produced from only a part of the living matter, while the other part

remains unchanged in the shape of a reticulum, or, still more probably, the myeline originates in a manner different from that of fat—viz., from the lifeless liquid contained in the meshes of bioplasson. In specimens of medullated nerve-fibers the myeline is often found exuded from the nerves in the form of numerous slightly refracting formations with a concentric striation, which is evidently caused by a slow oozing and aggregation of the myeline. (See Fig. 125.)

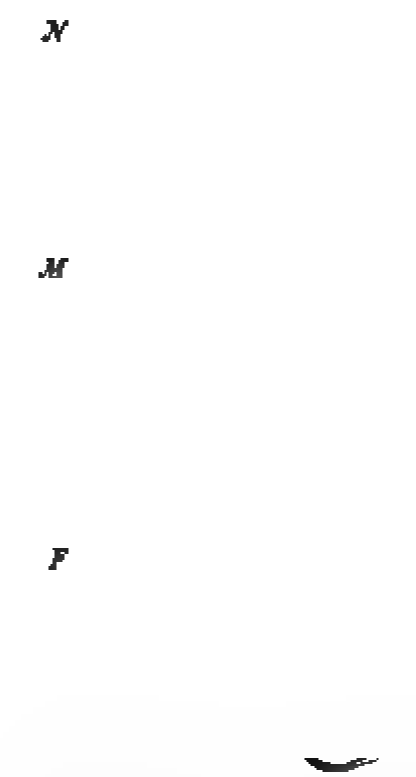


FIG. 125.—MYELINE DROPS, OOZED OUT FROM THE OPTIC NERVE OF A BULL.

N, bundle of medullated nerve-fibers; *M*, myeline drops. *F*, fat-granules. Magnified 400 diameters.

By staining fresh medullated nerve-fibers with a solution of nitrate of silver, the bundle was found to be covered by an endothelial coat. Each fiber exhibits a series of marks, which correspond to the "annular constriction" of Ranvier. The axis-cylinder at the point of constriction exhibits a number of dark brown transverse lines (Frommann). Between every two constrictions a transverse bar has been found, of a biconical shape, through the broadest portion of which the axis-cylinder passes. Ranvier concludes from these facts that each section of the nerve-fiber is a unit, a tubular cell, filled with myeline, like a fat-globule, which he terms the *interannular segment*, with an oblong nucleus in its investing membrane. The axis-cylinder, according to this author, pierces a series of interannular segments without interruption; while Engelmann, on the other hand, claims that each interannular constriction corresponds to an interruption of the axis-cylinder. This latter

assertion is contrary to our ideas of nerve action and so is the assertion o
other histologists, that the axis-cylinder is a fluid.

In peripheral formations of connective tissue—f. i., in the female breast, the derma of the skin, etc.—we often encounter single medullated nerve-fibers, exhibiting the characteristic features just described. Their double contour is due to the presence of the myeline sheath, and not to the refraction of the myeline, for the double contour is visible even when the myeline is absent. The fluted appearance of medullated nerve-fibers is partly due to

FIG. 126.—MEDULLATED NERVE-FIBERS OF THE FEMALE BREAST.

N, nerve-fibers; *C*, capillary blood-vessels, *F*, fat-globule with vacuoles. Magnified 600 diameters.

the presence of the oblong nuclei in the myeline sheath, and partly to constrictions along the course of the nerve-fiber, to the presence of which Remak, and recently Schmidt, drew attention, the nature of which is not yet understood. All these features are marked characteristics of medullated nerve-fibers, in contra distinction to those of capillary blood-vessels. (See Fig. 126.)

In nerve-bundles no ramification of the fibers takes place, but as they approach the periphery, either motor or sensitive, they branch very freely, and one fiber often splits into a number of slightly thinned branches.

(b) Non-medullated Nerves. These nerves have the appearance of being bare axis-cylinders, destitute of a myeline investment. There are comparatively broad so-called Remak's fibers (1838), in large numbers, in the sympathetic and in the cranial portions of the olfactory and auditory nerves. These fibers exhibit on their surface a number of oblong nuclei, and they have often a delicate sheath, kindred to the axis-cylinder sheath of medullated nerve-fibers, to which, probably, the nuclei belong. These nerves are described as indistinctly fibrillar in structure, and at certain intervals showing clusters of small, bead-like formations, giving rise to the so-called necklace appearance. All nerves in the earliest stages of embryonal development are non-medullated.

Besides these broad non-medullated nerve-fibers, there are others which are narrower, scattered throughout the gray substance of the brain and of the spinal cord. They run in bundles with the medullated nerve-fibers, and also with nerves of the sympathetic system. Such fibers, which are bare axis-cylinders, represent the origin of all nerve-fibers, even of the medullated, in the gray substance. In many instances, the medullated fibers become again non-medullated upon approaching the periphery of the body.

With high amplifications of the microscope, some of the larger non-medullated nerve-fibers show distinctly a delicate reticular structure. Others exhibit a number of minute vacuoles in their interior; still others, and these are the finest nerve-fibers, have a homogeneous appearance and give no evidence of structure. (See Fig. 127.)

Many of the finest non-medullated nerve-fibers show oblong, varicose enlargements along their course, and bear the name of *varicose nerve-fibers.* The varicosities are certainly not post-mortem appearances, as they are visible in the perfectly fresh condition of nerve-specimens, as stated above.

3. Terminations of Nerves.

The manner in which the ultimate nerve filaments terminate in the tissues and at the periphery of the body is known only in part. There are two varieties, either terminations of medullated nerves as such, or terminations of non-medullated nerves. The latter are either continuations of originally medullated

nerves, which have become destitute of their myeline investment upon approaching the periphery, or they are non-medullated, sympathetic nerve-fibers.

(a) Termination of Medullated Nerve-fibers.

The *motor hill* of nerves controlling the action of muscles (see chapter on muscle tissue).

The *tactile corpuscles of Merkel* in the web of the feet of water-birds, in the trunk of the pig, etc. These are finely granular, distinctly nucleated, globular bodies, into which the axis-cylinder penetrates, and which are located in the upper layers of the derma or in the epithelium—f. i., in that of the external root-sheath of the tactile hairs. Sometimes two or more such corpuscles are attached to the medullated nerve-fiber.

The *tactile corpuscles of Meissner or Wagner* are present in the papillæ of the derma of the skin, often below the level of the

FIG. 127.—MEDULLATED AND NON-MEDULLATED NERVE-FIBERS FROM THE RETINA OF A BULL.

S^1, myeline sheath, with oblong nuclei and (S^2) transverse septa. The myeline oozed out. N, non-medullated nerve-fibers, with varicose enlargements. Magnified 600 diameters.

papillæ, and especially numerous in the tips of the fingers and toes. These are ovoid or globular formations, with transverse or spiral striations and oblong nuclei arranged in the direction of the striations. One or more medullated nerve-fibers enter the corpuscle at one pole. Sometimes two or more such corpuscles are clustered together; but the way in which the termination of the axis-cylinder is effected is unknown.

The *bulbs of Krause* are found in the conjunctiva, in the mucous membrane of the floor of the mouth and of the lips, of the soft palate and the tongue, in the glans penis and in the clitoris. They are ovoid or mulberry-shaped bodies, in which the

axis-cylinder terminates as a knob. Longworth found them in some conjunctivæ, but not in all, and saw their interiors filled with nucleated corpuscles. Waldeyer considers these bodies to be intermediate formations between the tactile and the Pacinian corpuscles.

The *corpuscles of Pacini* (discovered by Vater in 1741) are found in the subcutaneous tissue of the nipple, the palm of the hand, and the labia majora, in the periosteum, the mesentery, especially along the branches of the sympathetic nerve, and in many other places. They are oval or pear-shaped bodies, composed of numerous concentric strata, exhibiting nuclei. The medullated nerve-fiber upon entering this body becomes destitute

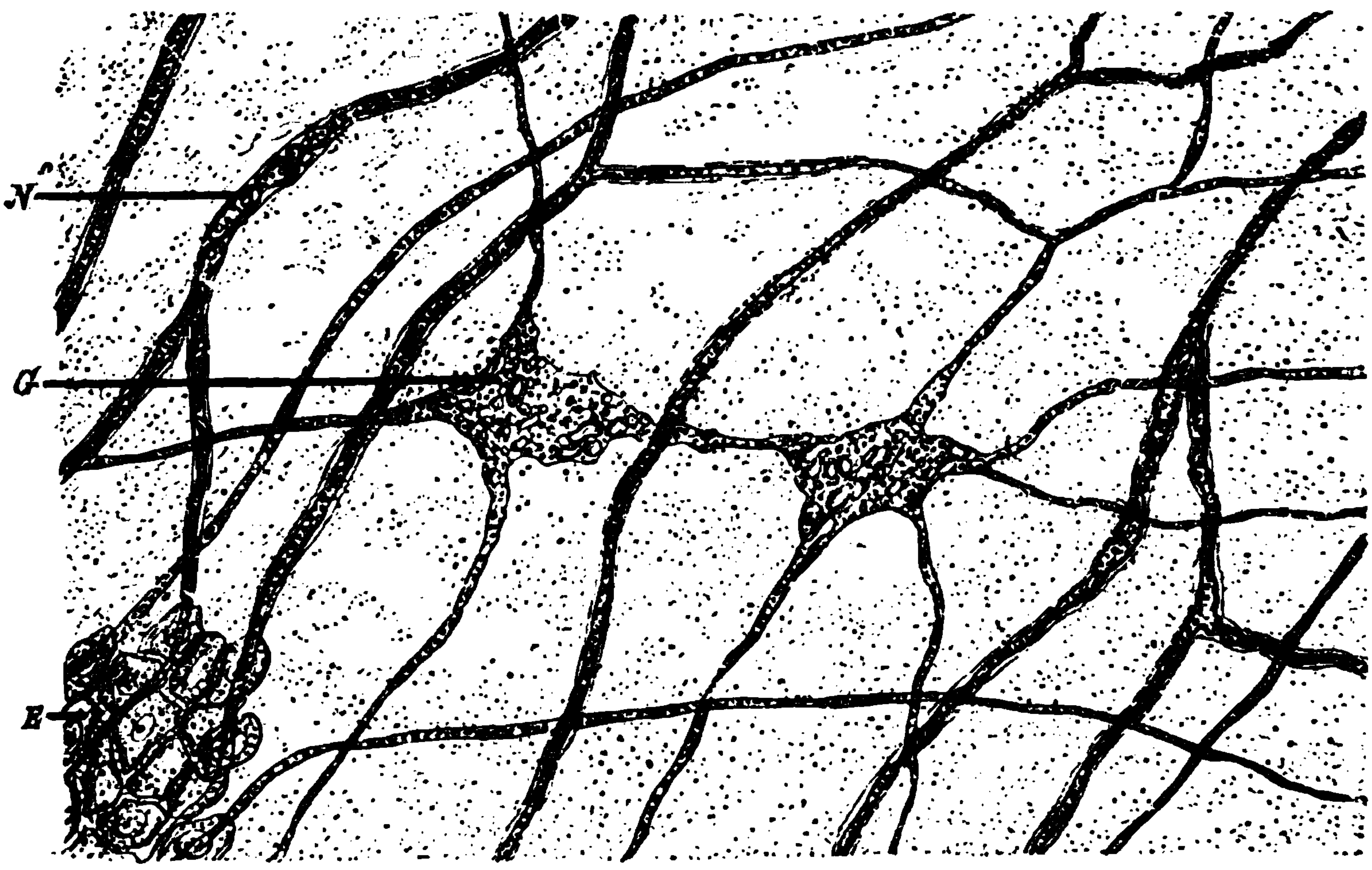


FIG. 128.—TERMINAL PLEXUS OF NON-MEDULLATED NERVES, BENEATH THE EPITHELIAL LAYER OF THE CORNEA OF A BULL.

N, non-medullated nerve-fibers, partly with a delicate reticular, partly with a lumpy, structure; *G*, ganglionic enlargement; *E*, columnar epithelia, in top view. Magnified 600 diameters.

of its myeline, and terminates in a knob or a chain of granules. Sometimes two nerve-fibers pass into the corpuscle. The significance of these formations is not understood.

(b) Termination of Non-medullated Nerve-fibers. The most common termination of nerve filaments is a plexus, in which, as a rule, ganglionic elements are found as nodular points of inter-

section. Such plexiform terminations are seen in different localities beneath the epithelia, in the submucous tissue, and in the connective tissue between the circular and longitudinal muscle-layers of the intestines. (See Fig. 128.)

The *plexus of Meissner* is located in the submucous layer of the intestine, and exhibits distinct ganglionic enlargements (see chapter on alimentary canal).

The *plexus of Auerbach* is found at the junction of the two muscle-layers of the intestine; it contains nodular ganglionic bodies with numerous nuclei (see chapter on alimentary canal).

The axis-cylinders, near their terminations, divide into extremely delicate *axis-fibrillæ* (M. Schultze), which are slender, beaded filaments, representing the bioplasson reticulum in an elongated direction. Their course in the cornea has been accurately studied by W. Hassloch (see page 175, Fig. 67). They enter a cornea-corpuscle and inosculate with its bioplasson reticulum, evidently in the same manner in which they originate in the central ganglionic element. Many fibrillæ simply pass through one corpuscle and enter another; fibrillæ have been also traced into the bioplasson reticulum of the basis-substance. Terminations of this kind are found in different connective-tissue formations; they are not permanent, but may occur from a temporary enlargement and elongation of reticular fibrillæ connecting with former nerves. As they are bioplasson formations, they may disappear by falling back into the reticulum.

The finest plexiform terminations of axis-fibrillæ are observed in the walls of capillary blood-vessels, particularly in the cement-substance between the endothelia (W. Tomsa and others). Such plexus formations were found in the epithelia by Pflüger, Langerhaus, and others, and it is still an unsettled question whether the nerves terminate in the cement-substance between the epithelia, or penetrate the epithelial bodies themselves.

Peculiar epithelial formations are the gustatory buds (Schwalbe) and the olfactory cells (M. Schultze), the connection of which with nerve-fibers, however, is still a disputed point. Very complicated formations are those of Corti's organ and of the retina. The plates, the "hair-cells," the rods and cones are well known, but how the nerves connect with these is unsettled. In the light of the bioplasson theory we may, at a time not far distant, hope for new discoveries and new views.

Development of Nervous Tissue.

Very little is known in regard to the development of the nerve-centers and the nerves. All observers adhere to the idea that the nerve-centers are products of the outer or horny embryonal layer, the epiblast. According to general biological views, this cannot be correct. The nerves, being so closely allied to connective tissue, are offspring developments from the middle embryonal layer, the mesoblast. L. Unger* maintains that the medullated nerve-fibers of the brain arise from radiating tracts, in which the cells are arranged in columns; these columns first have a reticular appearance and an investing membrane. He claims that the reticulum of the myeline layer is produced earlier than the axis-cylinder; that connective tissue and nerve-tissue may arise from one and the same cell, and that nerve-fibers or axis-cylinders may come from certain portions of the reticulum.

Fig. 129.—Brain of a Human Embryo, Five Weeks Old.

P, gray substance with numerous nuclei; *A*, axis-cylinders; *C*, capillary blood-vessels. Magnified 600 diameters.

My own observations prove that the brain of a human embryo five weeks old is composed of a bioplasson reticulum, whose points of intersection with low powers appear to consist of granules. In this reticular mass numerous nuclei are imbedded, and tracts of axis-cylinders laid before even a trace of a medullated nerve can be demonstrated. (See Fig. 129.)

This shows that the development of the nerves can never be understood in accordance with the cell theory, inasmuch as there

* "Untersuchungen über die Entwicklung der centralen Nervengewebe." Sitzungsber. d. Wiener Akad. d. Wissensch, 1879.

is nothing to support the assumption that nervous tissue originates from "cells." Unquestionably, there are large masses of reticular bioplasson in which by a growth of living matter, chiefly in one direction, axis-fibrillæ originate, while the medullary investment is a much later formation. At first there is no trace of ganglionic elements. We know that these elements make their appearance only after the third month of intrauterine life. The motor elements of the spinal cord particularly are first observed during the third and fourth months, corresponding to the time when the embryo begins to manifest signs of life. Further, the ganglionic elements cannot arise from cells, as they are no cells, but from portions of living matter arranged in clusters, in which all the plastids remain interconnected. This mode of development is indicated by the inflammatory changes of the ganglionic elements, when they return to their embryonal condition.

In the human embryo two months old, the intervertebral ganglion is composed of medullary tissue, with relatively large fields of myxomatous basis-substance. The nerves are non-medullated, which proves that the myeline investment must be formed at a later period than the axis-cylinder. (See Fig. 130.)

For a successful investigation of the development of nervous tissue the recognition of two points is, in my opinion, of fundamental importance—viz.: first, that the nervous system is a formation originating in the middle embryonal layer; and second, that no isolated "cells" take part in the production of nervous tissue. With the knowledge of these facts, we can understand that in an elongated group of interconnected plastids the central portion may remain unchanged living matter, the axis-cylinder; while a more peripheral portion may become reticular (horny?) and infiltrated with myeline as a kind of basis-substance, and that the most peripheral portion, by a solidification of the bioplasson liquid, may be transformed into the myeline sheath with a nucleus, in about the same manner as a fat-globule arises from myxomatous connective tissue.

Methods for the Preparation of Nerve-tissue.

Successful examination of the nerve-tissue depends on a suitable mode of preservation. Teasing, tearing, pulling, and making specimens "half dry" are methods unworthy of being named.

Small pieces of the brain or the spinal cord should be placed

in a dark wine-yellow solution of bichromate of potash, or in Müller's fluid. Either of these liquids should be greatly in excess compared with the bulk of the specimens. They will preserve the nerve-tissue, if changed every fourth or fifth day, or until the liquid remains clear. The hardening can be accomplished afterward by alcohol or a very weak (one-fifth to one-tenth per cent.) solution of chromic acid. A slight excess of chromic acid will soon render the nerve-tissue brittle and not suitable for sections.

FIG. 130.—INTERVERTEBRAL GANGLION OF A HUMAN EMBRYO, EIGHT WEEKS OLD.

O, partly solid, partly nucleated, plastids ; *N*, nerve-fibers, not yet medullated ; *M*, delicate myxomatous connective tissue ; *B*, capillary blood-vessel, cut transversely. Magnified 600 diameters.

Sections made with razor, or other cutters, are alone appropriate, in my opinion, for study of this tissue. The teasing of the tissue, which is unavoidable even with this mode of preparation, is the only teasing allowable, and may sometimes show noteworthy characters. The thinness of the section is its main value. By mounting in dilute glycerine the details will be

brought to view in a manner far surpassing specimens mounted in balsam.

Osmic acid (see page 9) may be used successfully. The most important of our present re-agents is the one-half per cent. solution of gold, by means of which J. Cohnheim * first succeeded in clearing up the termination of nerves in the epithelia of the cornea. From twenty to forty minutes' exposure to this solution renders all bioplasson formations distinct, although the specimens after five or six years become worthless, as they grow too dark for study. Treatment with acetic, lactic, tartaric, and formic acids assists the action of the gold-salt; but the proper use of these acids can be learned only by experience.

ANALYSIS OF BIOPLASSON IN ITS RELATIONS TO NERVE-ACTION.

Thoughtful minds for a number of years have anticipated the modern views concerning the function of the nervous system. I quote from L. Elsberg (*l. c.*, see page 185) the following historical data:

"According to Drysdale,† Dr. John Fletcher, of Edinburgh, was the first‡ who clearly abandoned the idea that the material elements of an organism require the addition 'of an immaterial or spiritual essence, substance, or power, general or local, whose presence is the efficient cause of life,' and who arrived at the conclusion that 'it is only in virtue of a specially living matter, universally diffused and intimately interwoven with its texture, that any tissue or part possesses vitality.' He denied vitality to any gaseous or purely liquid fluid, and any hard or rigid solid; and thought the only truly living matter consisted 'of the gray matter of the ganglionic nerves, which he held to be universally diffused, and the gray matter of the brain and spinal marrow.' He described it as a 'nitrogenous, pulpy, translucent, homogeneous matter, yielding, after death, fibrin.' 'Chemical analysis, accordingly, must be considered as useful in showing us, not what such matter *was composed of* while it possessed vitality, but what it is composed of *afterward*.' 'Not only is every vital action traced to molecular change, and to consumption and regeneration of this structureless, semi-fluid matter, combined in a way entirely *sui generis*, but the initiation of these changes is brought by Fletcher into absolute dependence on stimuli, and all spontaneity or autonomy is denied to matter in the living just as in the dead state.'

"As Fletcher's work was published in 1835, several years before even the establishment of the cell-doctrine, we cannot but agree so far with Drysdale as to say that Fletcher has framed a 'hypothesis of the anatomical nature of the living matter which anticipates in a remarkable manner' its discovery! In 1850, Cohn § recognized the protoplasm 'as the contractile

* Virchow's Archiv, Bd. 38.

† "The Protoplasmic Theory of Life," London, 1874.

‡ "Rudiments of Physiology," Edinburgh, 1835.

§ "Nachträge zur Naturgeschichte des Protococcus pluvialis." Nova acta Acad. Leop.-Carol., vol. xxii., part I., p. 605.

element, and as what gives to the zoöspore the faculty of altering its figure without any corresponding change in volume.' He concludes that protoplasm 'must be regarded as the prime seat of almost all vital activity, but especially of all the motile phenomena in the interior of the cell.' In 1853, Huxley* said: 'Vitality—the faculty, that is, of exhibiting definite cycles of change in form and composition—is a property inherent in certain kinds of matter.' In 1855, Unger† thought that 'the proximate cause of the movements of the sap in the cells is to be sought neither in diosmosis, nor in the action of the nuclear vesicle, nor in any mechanical contrivance, such as cilia, but it lies rather in the constitution of the self-moving protoplasm, which, as an especially nitrogenous body of the nature of that simple contractile animal substance called sarcode, produces the rhythmically advancing contraction and expansion.'

"In 1856, Lord S. G. Osborne discovered carmine staining, and distinguished, by means of coloring it, the living formative matter from the formed material—a means which has borne important fruits in the discovery of Cohnheim's staining of living matter by gold chloride, and in that of Recklinghausen's staining all except living matter by silver nitrate.

"In 1858, and in a number of later articles,‡ Max Schultze, by showing that, as had been hypothetically supposed by Unger, the movements of the pseudopodia and the granules are really produced by active contractile movements of the protoplasm, and by other observations, contributed much to the establishment of the theory of living matter. Hæckel has also for many years, and in various publications, § labored to maintain and extend the same theory, of which he thus expresses himself:‖ 'The protoplasm or sarcode theory, that is . . . that this albuminous material is the original active substratum of all vital phenomena, may, perhaps, be considered one of the greatest achievements of modern biology, and one of the richest in results.' And says Drysdale:¶ 'If the grand theory of the one true living matter was, as we have seen, hypothetically advanced by Fletcher, yet the merit of the discovery of the actual anatomical representation of it belongs to Beale, in accordance with the usual and right award of the title of discoverer to him alone who demonstrates truths by proof and fact. . . . The cardinal point in the theory of Dr. Beale is not the destruction of the completeness of the cell of Schwann as the elementary unit, for that was already accomplished by others. . . . But that, from the earliest visible speck of germ up to the last moment of life, in every living thing, plant, animal, and protist, the attribute of life is restricted to one anatomical element alone, and this homogeneous and struct-

* "Review of the Cell-theory." *British and Foreign Medico-Chirurg. Review*, October, 1853.

† "Anatomie und Physiologie der Pflanzen," 1855, pp. 280, 282.

‡ "Ueber innere Bewegungs-Erscheinungen bei Diatomeen," Müller's Archiv, 1858, p. 330; "Ueber Cornuspira," Archiv f. Naturgesch., 1860, p. 287; "Ueber Muskelkörperchen und das was man eine Zelle zu nennen habe," Reichert und Du Bois-Reymond's Archiv, 1861, p. 1; "Das Protoplasma der Rhizopoden und der Pflanzenzellen," Leipzig, 1863.

§ "Monographie der Radiolarien," 1862, pp. 89, 116; "Ueber den Sarcodekörper der Rhizopoden," Zeitsch. f. Wissensch. Zoologie, 1865, p. 342; "Generelle Morphologie," vol. i. pp. 269, 289.

‖ "Monographie der Moneren," Jenaische Zeitschft. f. Medicin und Naturwissenschaft. 1868, iv. 1; translation in *Quarterly Journal of Microscopical Science*, London, 1869, vol. ix., p. 223.

¶ *Loc. cit.*, p. 42, *et seq.*

reless; while all the rest of the infinite variety of structure and composition, olid and fluid, which make up living beings, is merely passive and lifeless ormed material. This distinction into only two radically different kinds of natter — viz.: the living or germinal matter and the formed material — gives he clue whereby he clears up the confusion into which the cell-doctrine had allen, and gives the point of departure for the theory of innate independent ife of each part, which the cell-theory had aimed at but failed to make good. The one true and only living matter — called by Beale germinal matter, or bioplasm — is described as "always transparent and colorless, and, as far as an be ascertained by examination with the highest powers, perfectly structreless, and it exhibits those same characters at every period of its existence." . . The living matter of Beale corresponds to the following histological ements of other authors: The viscid nitrogenous substance within the primordial utricle, called by Von Mohl protoplasm; the primordial utricle itself, in egeli's sense of that term — viz.: the layer of protoplasm next the cell-wall; transparent semi-fluid matter occupying the spaces and intervals between threads and walls of those spaces formed by the so-called vacuolation of toplasmic masses; the greater part of the sarcode of the monera, rhizola, and other low organisms; the white blood-corpuscles, pus-corpuscles, l other naked wandering masses of living matter; the so-called nucleus of secreting cells, and of the tissues of the higher animals, and many plantls; the nuclei of the cells of the gray matter of the brain, spinal marrow, d ganglions, and the nuclei of nerve-fibers. The term of true living or germal matter can never be given to the following parts, although to some of em the word protoplasm has been erroneously applied — viz.: the cell-wall plants or animals, however delicate or gelatinous; the threads or filaments nd walls of the vacuoles within protoplasmic masses or cells; the wall of the rimordial utricle; the true fibrous, connective, elastic, bony, or other tissues enerally included among the living parts of animals; even the proper conractile fiber of the muscles, the radiating fibers of the caudate nerve-cells, and the outer coat of those cells, besides the nerve-fibers in general; the hard parts of epithelial cells, and all liquid secretions; the cilia; the tissue of cuticle, hair, nails, horn, and all analogous parts in plants; the granules in sarcode; all coloring matter; and, lastly, all pabulum, including the fluid part of blood, lymph, and chyle, and corresponding matters in plants. In short, the name of bioplasm, given by Beale, or protoplasm (in a restricted sense, as it will probably be ultimately accepted by biologists), as indicating the ideal living matter, cannot be given to any substance displaying rigidity n any degree, from the softest gelatinous membrane up to the hardest teethnamel; nor to anything exhibiting a trace of structure to the finest microcope; nor to any liquid; nor to any substance capable of true solution. hus, "nothing that lives is alive in every part," but as long as any individal part or tissue is properly called living, it is only so in virtue of particles of he above-described protoplasm freely distributed among or interwoven with he textures so closely that there is scarcely any part one five-hundredth of an nch in size but contains its portion of protoplasm. Thus we see realized the ypothesis of Fletcher — that all living action is performed solely by virtue of portions of irritable or living matter interwoven with the otherwise dead textures. According to Beale, "of the matter which constitutes the bodies of men and animals in the fully formed condition, probably more than four-fifths are in the formed and non-living state. All this was, however, living at an

earlier period of existence." This is on an average, for some tissues contain much less living matter; the bones, for example, only one-twentieth, and some textures, when old, not more than one-hundredth.'

"I have made this long quotation from Drysdale's book, because I am anxious to do full justice to Beale, and I could not find a statement of his views so succinct for quotation in his own writing. The objection, however, urged by Bastian to Beale is so very pertinent that it must also find a place here, but I shall not dwell upon other points on which Beale differs from the bioplasson doctrine; such as that living matter exhibits the same characters at every period of its existence, and that it is always perfectly structureless. 'It has always appeared to me,' says Bastian,* 'to be a very fundamental objection to his theory, that so many of the most characteristically vital phenomena of the higher animals should take place through the agency of tissues — muscle and nerve, for instance — by far the greater part of the bulk of which would, in accordance with Dr. Beale's view, have to be considered as *dead* and inert.'"

Meynert's view — that the cortex of the brain is a mirror, on which, by means of the conducting nerves, impressions from the outer world are projected — has in late years decidedly gained ground. He found that the nerves of the special senses go to special convolutions of the cortex of the brain, and that from other convolutions arise nerves which control muscle action. Hitzig was the first who discovered points in the cortex of the brain of the cat, which, upon being stimulated by electricity, produced regularly recurring motions in the extremities. Later, Ferrier and Munk demonstrated in the brain of apes the isolation of special sensory perception and of muscular movements, usually subject to the will. Their experiments confirm the anatomical premise of Meynert in its general bearings. It was found that, by cutting away a certain part of the brain of these animals, blindness would result, while the removal of another part was followed by deafness, and of still another by paralysis. If the latter parts, instead of being removed, were stimulated by electricity, special motions followed, as if they were produced by the will of the animal. These observers found the keys of the mind of the animal in the gray substance of the convolutions of the brain, and, by touching a special key, could simulate the expression of the animal's feelings.

Pathological processes in the brain have greatly aided in corroborating the localized nature of sensory and motor functions. Meynert especially pointed out the center of speech by the study of aphasia, which is a loss of the power to pronounce certain words. This center is in the Reil's island, with the claustrum outside the third member of the lenticular nucleus. Meynert pointed out, in a series of careful researches, that the claustrum is a component part of the cortex of the island, the cortex around the fossa Sylvii, and the posterior orbital convolution. It represents the fifth layer of the cortical structure, which is more than usually developed and serves for a broad connection with other territories of the cerebral cortex. The connection of the claustrum with an auditory bundle renders the walls of the fossa Sylvii a field for sound, while the connection of the claustrum with the fibrous systems of the medulla of the island of Reil and the external capsule of the lenticular nucleus renders this field of sound a central organ of speech. Aphasia depends on a destruction or a

* "The Beginnings of Life: being some account of the Nature, Modes of Origin, and Transformations of Lower Organisms." London, 1872, vol. i., p. 155.

rbid change of ganglionic elements in this center. Such facts, compared h the appearance of muscular movements in the embryo upon the formation

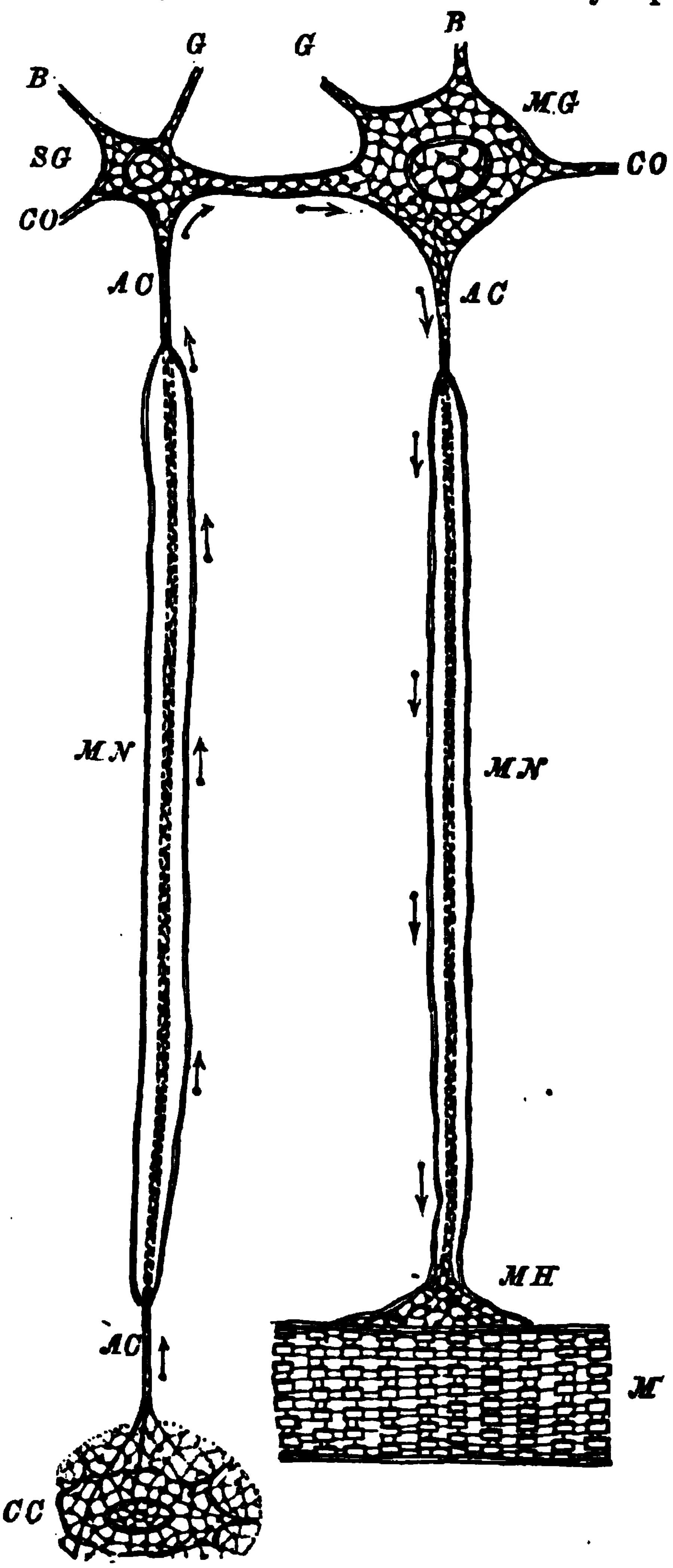


FIG. 131.—DIAGRAM OF NERVE CONDUCTION.

MG, motor ganglionic element; *SG*, sensitive ganglionic element; *G*, offshoot to the gray ubstance of the spinal cord; *B*, offshoot to the gray substance of the brain; *CO*, offshoot o analogous ganglionic elements for coördinate sensation and motion; *AC*, axis-cylinder, ransformed into *MN*, a medullated nerve-fiber; *CC*, cornea corpuscle in connection with he sensitive ganglionic element; *M*, striped muscle, with *MH*, the motor hill, in connection rith the motor ganglionic element.

of motor ganglionic elements in the spinal cord, would also indicate that every group of muscles has, to a certain extent, independent centers in the gray ubstance.

The hypothesis becomes, perhaps, admissible that all we call positive concrete knowledge—f. i., 1, 2, 3, etc., or *a*, *b*, *c*, etc., primarily gained by sense impressions—is localized in special ganglionic elements, while abstract or general nervous activity rests in the diffused, nucleated portions of the gray substance between the ganglionic elements. Such diffused activities are: hope, fear, imagination, dreaming, etc. The increase of knowledge throughout life would mean that there was a corresponding new formation of ganglionic elements. Intelligence could depend chiefly upon the number of these elements, and their number could be increased by education and by learning. Memory could be based on the grouping of bioplasson particles, which at certain times might be brought into motion, and again might return to relative rest.

Nervous action, perhaps, depends entirely upon a contraction of the bioplasson reticulum. Should such a contraction be induced on the periphery of the body, it would be conveyed to the center, and recognized as pain; if, on the contrary, contraction start in the center and be conducted to the periphery, it would result in muscular movement. From this point of view the designation of sensitive and motor nerves becomes superfluous, for experiments have already proved that the same nerve can at one time be a sensitive, at another time a motor, conductor. We need only assume sensitive and motor stations in the centers, in connection with each other. What the motor agent is which causes movement in the bioplasson reticulum of the central organ, as well as throughout the whole organism, we do not know, and consequently are at liberty to give it any name. As regards the spinal cord, the nerve action seems to be sufficiently plain. (See Fig. 131.)

Reflex action, coördinate sensation, motion, and conduction from and to the brain take place in separate routes, which must be in connection with the sensitive and motor ganglionic elements by means of offshoots. The multipolar form of these bodies, perhaps, may be accounted for in this way.

X.

EPITHELIAL AND ENDOTHELIAL TISSUE.

THE ideas concerning the character of epithelium and endothelium, as presented here, are widely different from the opinions usually held upon this subject. The light of the bioplasson theory has been brought to bear upon a subject hitherto but little understood. All the views here advanced have been taught by me in my laboratory for over seven years, and these views were in part published in 1878.*

Definition. A single living plastid,—for instance, an amœba, a colorless blood-corpuscle, or a pus-corpuscle,—with high magnifying powers of the microscope, exhibits a delicate, net-like structure, both within the nucleus and in the surrounding body. The body is inclosed by an extremely thin, shining, homogeneous layer, and a layer of this kind always lines the vacuoles seen, temporarily or permanently, in a creeping plastid. The net-work of the body inosculates with both the peripheral layer and that inclosing a vacuole. The reticulum of the nucleus, its surrounding envelope—the net-work of the plastid, the covering and lining layers, both of the body and its vacuoles, are formations of living matter, the active contraction and passive extension of which cause locomotion and all changes of form during the life of the plastid.

In the germinal disk of the more highly developed animals, which arises from two symmetrical halves of the impregnated

* "Epithelium and its Performances." A paper read before the American Dermatological Association, at their meeting in Saratoga, August 27, 1878. Published in abstract. *New York Medical Journal*, 1878.

germ, indicative of the symmetrical halves of the future organism, three layers are recognized. The so-called mesoblast, the layer which forms the main bulk of the germinal disk, is covered on its outer surface by a thin layer of flattened plastids, termed the epiblast; the under surface of the mesoblast is also covered by a similar layer, which is termed the hypoblast. In the mesoblast the first-formed vacuole, the future heart, is lined by a thin, continuous layer, which is connected with all surrounding plastids by means of delicate filaments. According to our ideas, the mesoblast must give rise to the principal part of the organism, composed of connective tissue, of muscles, and of nerves. The nerve-layer is closely attached to the epiblast, and this is the reason that, since Remak's time, it has been considered a formation of the epiblast. Such a conception, however, cannot be correct, as the nervous system is largely intermixed with connective tissue, carrying blood-vessels, and these latter formations never appear in the derivations of the epiblast and hypoblast—*i. e.*, the *epithelia.* The thin layer around the first-formed vacuole is the representative of all the future lining investing layers of closed cavities, and furnishes in the developed organism the tissue termed *endothelium.*

All formations in a highly developed animal body which are analogous to the outer or covering layer of a single plastid—that is, those which cover the external surface of the body and line all the inner cavities in direct or indirect connection with the outer surface—are termed *epithelia.* Formations, on the contrary, which are analogous to the wall of a closed vacuole of a single plastid, bear the name of *endothelia. Epithelia* are found: *On the outer surface of the body,* the skin and its appendages: the hairs, nails, sebaceous, sudoriparous, and mammary glands; the crystalline lens of the eye; in the system known as the *gastro-intestinal tract* and its prolongations, the mucous and salivary, pepsine and intestinal glands, and the liver; in the cavity of the *respiratory tract* and its mucous glands; and in the cavities and canals of the *genito-urinary tract,* including all its prolongations into the kidneys and the genital glands. *Endothelia* line the *closed cavities of the skull and the spine,* all its covering membranes, and *all ventricles in the brain* and their prolongation into the spinal cord; the *cavities of the chest,* both pleural and pericardial; the *cavity of the peritoneum; all articulations,* and all *blood- and lymph-vessels,* including the cavities of the heart.

This distinction was first established by His, who, at the same

time, maintained that the epithelia were an offspring of the epiblast and the hypoblast, while the endothelia were formations of the mesoblast, and closely allied to connective tissue. A perfect distinction between epithelia and endothelia, however, cannot be carried out for two reasons. *First:* The history of development and the scheme of a single plastid demonstrates that both epithelia and endothelia are originally flat layers of living matter, which split up into plastids, the only difference between them being that the epithelial layer is on the surface of the body, while the endothelial layer lines closed cavities in the interior of the body. *Secondly:* There is a direct communication between epithelia and endothelia at the openings of the uterine tubes into the peritoneal cavity; the epithelial formations of the ovaries are in no communication with the outer world; the crystalline lens, which is in its nature a formation completely epithelial, is covered by the endothelium of the anterior and posterior chambers of the eyeball; the epithelia of the liver join the endothelia of the capillaries, and are in direct connection with them. Further, epithelia and endothelia are identical in their intimate structure. Again, there exist single epithelial layers in the body—f. i., those of the bile-ducts, the salivary glands, the uriniferous tubules; and, on the other hand, ciliated endothelium is also found in the ventricles of the brain and the central canal of the spinal cord, etc., etc.

Epithelia and endothelia represent continuous investing layers of living matter. The former are the earliest formations in a developing body, after the stage of indifference introduced by the segmentation of the impregnated germ is passed. The latter are formations, starting with the appearance of vacuoles in the middle layer of the germ, the future heart and vessels. Both epithelia and endothelia are devoid of blood-vessels and lymphatics.

Structure. The epithelial and endothelial layers are constructed of single polyhedral plastids, the formerly so-called "epithelial and endothelial cells." Each plastid is separated from its neighbors by a narrow cloak of a lifeless, horny cement-substance, which is closely allied to the basis-substance of the connective tissue, but is not glue-yielding. Concerning the chemical constitution of these substances nothing is determined. Under the microscope we can see only the lateral portions of the envelope, which has the appearance of a pale seam around each polyhedral body. (See Fig. 132.)

The *net-work of living matter within the plastids sends delicate conical offshoots through the cement-substance, both in epithelia and*

endothelia. These offshoots, up to the present time, were termed "thorns of Max Schultze," in honor of their discoverer. This observer, in 1864, described thorny or prickle cells in the epithelia of the conjunctiva, the lips, the tongue of children, which, on being isolated, exhibited rows of prickles, constituting the appearance of "ridged cells." He knew that the prickles were conical in shape, and in two adjoining epithelia so arranged as to resemble two cog-wheels, the teeth of which are pressed into each other, but expressed no positive opinion as to their significance. Later observers, though their number was very great, did not settle the question of the nature of the prickles. The only fact admitted by all was that the prickles were very marked in epithelia taken from localities which were subject to an irritation or inflammation. In 1873, I declared the prickles to be formations

FIG. 132.—ENDOTHELIAL INVESTMENT OF THE PERITONEUM OF A CHICKEN, SLIGHTLY STAINED WITH CHLORIDE OF GOLD.

E, polyhedral endothelia, separated from each other by light rims of cement-substance, interconnected by delicate filaments; *SS*, stomata in the cement-substance; *BV*, capillary blood-vessel lined by endothelia, seen in edge-view; *BC*, blood-corpuscles. Magnified 600 diameters.

of living matter, traversing the rims of the cement-substance and interconnecting like bridges all epithelial and endothelial bodies (see page 130). That the thorns are of universal occurrence in the cement-substance and formations of living matter, can be proved by different chemical re-agents and by the study of pathological conditions, such as inflammation, fatty degeneration, etc. In inflammation, and in certain tumors, an active new growth of living matter starts from these filaments, which leads

to the formation of inflammatory corpuscles, and also of new epithelia (see papilloma in chapter on tumors).

One of the favorite subjects for the study of endothelium was the *peritoneum*. The same valuable re-agents which have been of so much service in elucidating the minute structure of the basis-substance of connective tissue, have also proved useful for the revelation of the structure of the cement-substance. These re-agents are the nitrate of silver and the chloride of gold. Von Recklinghausen had demonstrated that the cement-substance, under the influence of a one per cent. solution of nitrate of silver, becomes dark brown, and that in the endothelia of the lymph-sacs and that of the peritoneum circular openings appear, which lead into the lymphatics, and in a very short time admit of the absorption of fine granules of carmine, aniline, etc., injected into the

FIG. 133.—ENDOTHELIAL INVESTMENT OF THE PERITONEUM OF A CHICKEN, STAINED WITH NITRATE OF SILVER.

K, knobs of small endothelia, along the blood-vessels; *V*, capillary blood-vessels, coursing in *C*, the connective-tissue layer of the peritoneum. Magnified 150 diameters.

cavities. The so-called serous surfaces proved to be closed lymph-sacs, which are in an open communication with the lymph-vessels. It became known that the endothelia of the peritoneum are of varying sizes, and E. Klein demonstrated knob-like protrusions along the blood-vessels, connected with the growth of the endothelia. (See Fig. 133.)

The two surfaces of the free peritoneal membranes—f. i., the omentum, the mesentery—exhibit endothelia differing in size,

the endothelia which directly cover the capillary blood-vessels being decidedly larger than those covering the delicate interstitial fibrous connective tissue. After staining with silver, solid dark brown, circular spots appear in the brown basis-substance, and are far more numerous in the endothelia between, than in those above blood-vessels; or there are simple ring-like formations, or light openings, surrounded by a wreath of small endothelia. The openings at the angles of the polyhedral bodies are termed stomata; those in the middle of a brown line of cement-substance, stigmata, both being essentially identical—viz.: openings of the lymphatics. Similar formations were found also in the endothelial layer of capillary lymph- and blood-vessels, and J. Arnold drew attention to their largely increased number in the blood-vessels of inflamed tissues, indicating an active emigration of colorless blood-corpuscles.

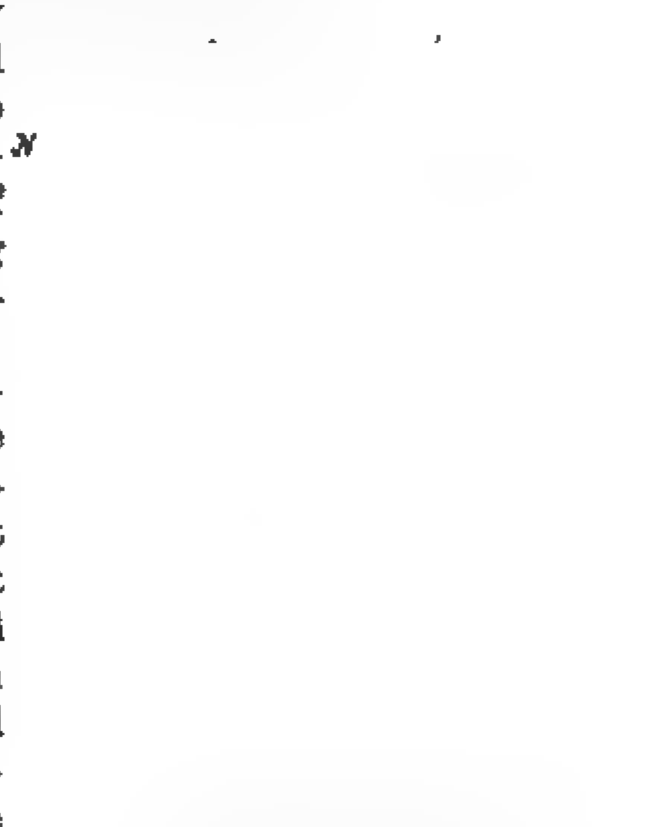


FIG. 134.—ENDOTHELIAL INVESTMENT OF THE PERITONEUM OF A PUP, STAINED WITH NITRATE OF SILVER.

N, nuclei faintly visible in the endothelia; *C*, dark brown, interrupted lines of cement-substance; *SO*, stomata at the angles; *SI*, stigmata in the middle of the brown lines. Magnified 800 diameters.

In thin specimens of silver-stained endothelia the dark brown cement-substance is never smooth, but more or less fluted, and at regular intervals traversed by delicate light lines, which unquestionably correspond with the "thorns" or filaments not affected by the silver salt. (See Fig. 134.)

The *crystalline lens* is known to be a formation of the horny germ-layer, the epiblast; it is, therefore, an epithelial structure, composed of flat ribbons, which are arranged in a peculiarly radiating and concentric manner. The peripheral ribbons are possessed of oblong nuclei. Delicate fringes have been noticed along the edges of torn ribbons of the lens, but their significance was not understood. They are the same formations as exist in all epithelia—viz., Max Schultze's "thorns," the connecting filaments of the ribbons. The reticular

structure is easily recognized in each ribbon, in both fresh specimens and those preserved in a solution of chloride of gold or chromic acid. The nature of the cement-substance between the ribbons is made apparent by treatment with a solution of nitrate of silver, which colors it dark brown, and at the same time leaves delicate, light, conical lines unstained, as is the case in all other formations of cement-substance. (See Fig. 135.)

The connecting filaments in the cement-substance, owing to their extreme delicacy, are often imperceptible in fresh preparations, and even in specimens preserved in chromic acid sometimes only a delicate granulation is visible in their place. To render these filaments distinct, the staining with a one-half per cent. solution of chloride of gold must be resorted to. Epithelial formations are, as a rule, very slowly colored by the gold-salt, as the ensheathing envelope of the cement-substance seems to inter-

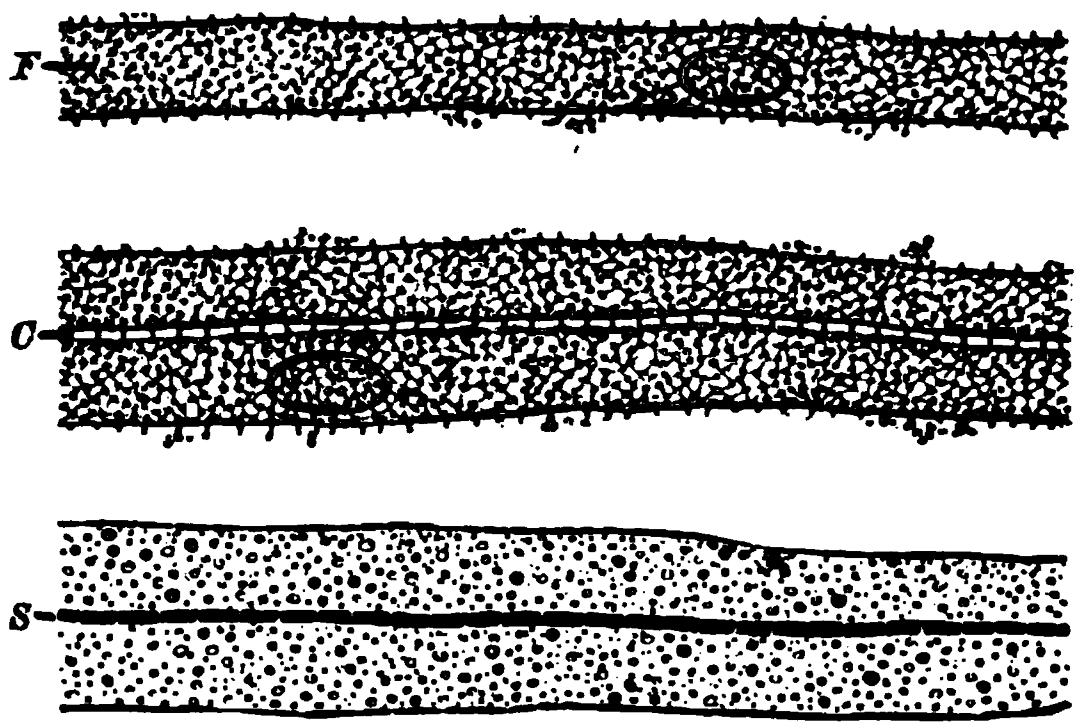


FIG. 135.—RIBBONS OF THE CRYSTALLINE LENS OF A BULLOCK.

F, isolated nucleated ribbon of reticular structure, and with fringed edges; *C*, two ribbons separated by the light cement-substance, interconnected by delicate conical filaments; *S*, two ribbons, stained with nitrate of silver; the cement-substance dark brown, pierced by light lines. Magnified 600 diameters.

fere with the action of the re-agent on the bioplasson reticulum in the interior. But the conical filaments in the cement-substance, if exposed to the re-agent for twenty to forty minutes, assume a violet color, and are rendered clearly visible.

The cloak of cement-substance is not of uniform hardness; it is probably more liquid in some places than in others, as indicated by the observations of J. Arnold, who drove colored injection liquids into the middle of the cement-substance. According to Thoma, an indigo-carmine solution being brought in repeated

small doses into the blood of a living frog will, after a short time, appear in the cement-substance of columnar and different stratified epithelia, the latter themselves exhibiting no trace of the coloring matter. Excavations in the cement-substance seem to be a necessity for the process of nutrition of the epithelia. In inflammation the cement-substance becomes liquefied, and thereupon admits of a free growth of the filaments and a coalescence of neighboring epithelia into multinuclear bioplasson masses. In the cement-substance of the epithelia of the liver there are regular tubular excavations, the bile-capillaries.

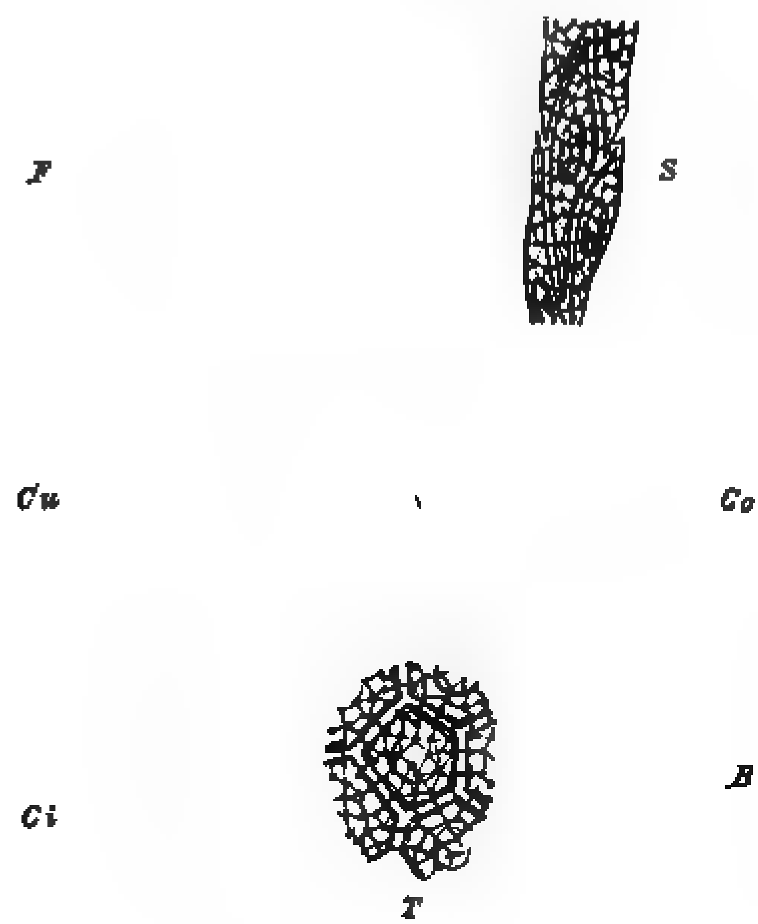


Fig. 136.—Diagram of the Varieties of Epithelia.

F, flat epithelia in front view, *S*, same in side view, *Cu*, cuboidal epithelia, *Co*, columnar epithelia in side view; *T*, columnar epithelia in top view, *Ci*, ciliated columnar epithelia; *B*, bacillated columnar epithelia.

Division. We distinguish mainly three varieties of epithelia—*the flat, the cuboidal, and the columnar or cylindrical,* the difference depending upon the prevailing diameter. (See Fig. 136.)

Flat epithelia exhibit a broad front surface, while in edge view they are spindle-shaped, because of the gradual narrowing from the middle portion, containing the nucleus, toward the periphery. The cuboidal epithelia derive their name from having

about the same diameter in all directions; while the columnar epithelia are elongated in one direction—viz., that vertical to the subjacent connective tissue. The cement-substance completely envelops the body of the epithelium.

Columnar epithelia have two sub-varieties—viz., *ciliated epithelium*, with moving, hair-like prolongations on the outer surface, and *bacillated epithelium*, provided with motionless, short, delicate rods, such as are found in the intestinal canal and the bile-ducts.

Columnar, ciliated epithelia usually occur in single layers; sometimes, however, the plastids inserted between the feet of the columnar epithelia are so numerous, and the wedged formations so regularly arranged, as to give the appearance of stratified columnar, ciliated epithelium—f. i., in the larynx, the trachea, the larger bronchi, the mucosa of the nasal cavities. The basis of the epithelial body—*i. e.*, the broadest outer surface—is supplied with delicate bent hair-like formations, which, during life, and for a short time after the removal of the epithelia from the body, have a waving motion, in a direction corresponding to the concave side of the hairs. Max Schultze has observed that the cilia penetrate the investing shell of the cement-substance, and are visible in the interior of the epithelium. Th. Eimer and E. Klein have demonstrated that the cilia, penetrating the outer shell, are in connection with the net-work within the epithelium. This fact I can fully corroborate. It explains the motion of the cilia in a satisfactory manner. The reticulum during life is never in perfect rest, and as each hair is attached to the reticulum by its short arm, while the long arm projects freely, the horny cement-substance representing the fulcrum of the lever, a slight pull on the short arm must result in a marked extension of the free long arm. This excursion will be most evident in the direction of the concavity of the cilium, each one being slightly curved. It also becomes explicable why liquids, slightly stimulating the living matter, increase the motion of the hairs, and make them move actively, even after they have become apparently inert. This delicate motion in one main direction is of importance in carrying foreign bodies or secretions outward, and other substances inward. The motion in the air passages—f. i., tending upward—will greatly assist in the elimination of mucus, which, collecting on the most sensitive portions of the larynx, the inner surface of the posterior wall, and the under surface of the vocal bands, produces reflex action, such as hawking, cough-

ing, etc. The motion of the cilia, in the cavity of the uterus, tending toward the mouths of the tubes, will assist the spermatozoids in reaching the ovum; while the motion in the Fallopian tubes, leading downward, will carry the ovum into the cavity of the uterus.

In man, ciliated epithelia are found in only a few localities. They exist in the respiratory portions of the nasal cavity; in the Eustachian tubes; in the labyrinth (hair-cells); in the larynx, beginning from the under surface of the epiglottis, with the exception of the vocal bands; in the trachea, the bronchi, and bronchioli; also in the ejaculatory ducts and the vas deferens of the male, and in the uterus and the Fallopian tubes of the female. (See Fig. 137.)

FIG. 137.—CILIATED COLUMNAR EPITHELIA, FROM THE NASAL CAVITY OF MAN.

E, row of columnar epithelia, *E*¹, detached epithelia, *P*¹, irregularly shaped plastids wedged in between the feet of the epithelia; *C*, connective tissue, bounded toward the epithelia by a light seam; *S*, the basement membrane. Above this a flat layer of endothelia is visible. Magnified 500 diameters.

In lower animals, the ciliated epithelia and endothelia are far more abundant; in the frog, for example, they are present in the cavity of the throat, the pericardiac sac, etc. An easily accessible place for obtaining ciliated epithelia, exhibiting acute movements, is the seam of the mantle of the oyster. Open the valves, cut off a small portion from the most pigmented seam, transfer it to the slide with a small drop of the juice of the oyster, and cover with a very thin covering-glass.

The feet of the columnar epithelia—that is, the extremities opposite the basis, and serving for attachment to the subjacent connective tissue—are sometimes blunt, sometimes very thin and curved, with bifurcations or indentations. The latter feature, especially in the juvenile condition of the epithelia, is due to the presence of relatively small, many-shaped plastids, which

appear partly homogeneous or partly nucleated, with offshoots. These indifferent corpuscles are evidently the starting material for newly growing epithelia. The connection of these wedged plastids *in situ* is accomplished by delicate filaments, which traverse the surrounding rims. The filaments themselves often increase in bulk and give rise to new epithelia.

Ciliated endothelia are met with in the investment of the ventricles of the brain and their continuation, the central canal of the spinal cord, *i. e.*, the so-called ependyma of Purkinje; and also on the surface of the plexus choroidei of the pia mater. In children their presence is invariable, but in adults they are not found in every case. In the central canal of the spinal cord the

FIG. 138.—CENTRAL CANAL OF THE SPINAL CORD OF A CHILD. TRANSVERSE SECTION.

E, wreath of ciliated endothelia, in connection with the subjacent connective-tissue; *N*, nerve-fibers of the anterior commissure; *W*, white substance; *F*, floor of the anterior longitudinal fissure, covered with flat endothelia. Magnified 300 diameters.

ciliated endothelia have a radiating arrangement, and in the posterior wall of the canal exhibit a gradual decrease in size toward the median line, where a slight fissure is observed. Here the cement-substance between the endothelia and also their nuclei are, as a rule, but slightly marked, while the cement-layer at the base of the endothelial wreath is quite broad. (See Fig. 138.)

Single epithelial layers may exhibit any of the above-named forms (flat, cuboidal, columnar); in the uriniferous tubules, for instance,

we find all varieties, according to the calibers of the tubules. *Stratified epithelial layers are composed of all the three forms.* Such stratified epithelia are found: on the surface of the skin, the oral cavity, the throat, the œsophagus, and the lowest portion of the rectum; also, in the lowest portion of the nasal cavities, on the upper surface of the epiglottis, on the vocal bands; further in the vagina, the cervical portion of the uterus, the urethra, the bladder, the ureters, pelves, and calices of the kidneys; lastly, on the conjunctiva, the outer surface of the cornea, the lachrymal ducts, the external auditory canal, the outer surface of the tympanum, and the Eustachian tubes, at their mouths in the cavity of the throat. Wherever stratified epithelial formations occur, the flat variety invariably composes the outer layers; the cuboidal, the middle layers, and the columnar the lowest layer, nearest to the connective tissue. In places where two stratified epithelial layers come in contact, there is often found between them an apparently structureless layer, the horny or cuticular layer, so-called in contradistinction to the basement layers, which exist between epithelia and connective tissue. Cuticular formations are seen in many places between the layers of flat and cuboidal epithelia in the skin; quite regularly between the inner root-sheath and the hair, and between the inner and outer root-sheaths of the hair. The cement-substance in stratified epithelium is always marked and traversed by delicate filaments, especially plain in places which are the seats of slight irritation. (See Fig. 139.)

The nuclei of the epithelia, particularly of the cuboidal, in thin sections are liable to drop out, leaving a vacuole. In the flat epithelia the nuclei and the body of the plastid are finely granular—viz.: the living matter has decreased, and the horny substance—a derivation from the bioplasson liquid—increased in amount. The nucleus, or the nucleolus, even in flat epithelia —f. i., of the oral cavity—may exhibit, under certain circumstances, the characteristics of living matter (Stricker). The flat epithelia of the most external part of the skin and those of the nails and hairs become deprived of nuclei and of life, and are transformed into a dry, horny material.

R. Heidenhain has drawn attention to the presence, in the interior of epithelia, especially kidney epithelia, of delicate, rod-like formations. Their significance will be spoken of in the chapter on the kidneys.

The attachment of epithelia and endothelia to the connective tissue is either direct, by means of delicate filaments penetrating

the rim between the feet of the epithelia and the neighboring fibers of connective tissue; or it is indirect, by means of an intervening basement layer. The latter is probably pervaded by a bioplasson reticulum (I have seen it in Bowman's layer of the cornea of the cat), which inosculates with that of the epithelia. Basement layers, however, are not constant formations; they are sometimes broad, sometimes narrow, and sometimes altogether absent, in one and the same organ in different persons. The outer surface of the basement membrane, in many instances, is found to be covered by a layer of flat, polyhedral bodies discovered by V. Czerny, by means of silver-staining. These bodies are classed among endothelia.

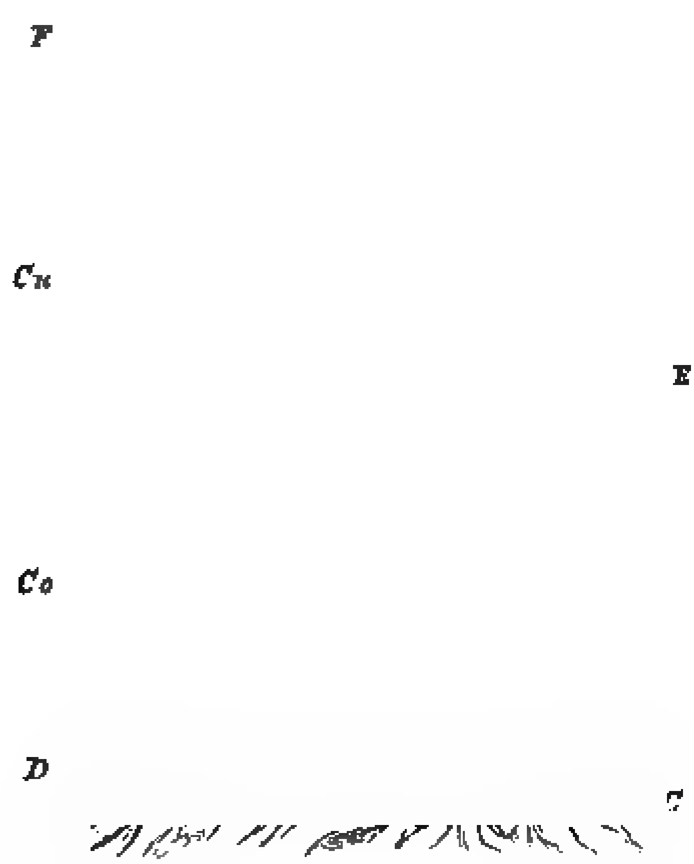


Fig. 139.—Stratified Epithelium of the Skin, Covering a Myxo-fibroma on the Right Shoulder. Vertical Section.

F, flat epithelia, *Cu*, cuboidal epithelia; *Co*, columnar epithelia, all the three composing the epithelial layer, *E*; *D*, derma of skin, composed of vascularized connective tissue, *C*. Magnified 600 diameters.

Termination of Nerves. Since Cohnheim's researches, we know that the finest axis-fibrillæ of the nerves terminate in the epithelial layers. The termination was described by some observers as a plexus between the epithelia, while others (Pflüger, Flemming) claim that the axis-fibrillæ penetrate the body of the epithelium, and may terminate in its nucleolus. My own observations enable me to state that the axis-fibrillæ — which, in specimens stained

with chloride of gold, can be recognized by their beaded appearance and their dark violet color — run in the cement-substance between the epithelia, and in this situation are in direct union with the filaments ("thorns") interconnecting the bioplasson reticulum of neighboring epithelia. (See Fig. 140.) In

FIG. 140.—DIAGRAM OF TERMINATION OF NERVES IN EPITHELIAL LAYERS.

AC, axis-cylinder, dividing into axis-fibrillæ, *AF*, which penetrate the hyaline or basement membrane, *H*, and course in the cement-substance between the columnar epithelia, *CO*, and the cuboidal epithelia, *CU*. The axis-fibrillæ are directly connected with the transverse filaments in the cement-substance, and indirectly with the bioplasson reticulum of the epithelia.

this way, the active portion of the epithelia — the living matter — is controlled by the nerves. Here and there a beaded thread can be traced into the body of an epithelium, and this occurrence is easily understood if we bear in mind that the nerve-fibrillæ and the reticulum of living matter are, in essential points, identical formations. The only reliable means for tracing the nerve terminations is by chloride of gold staining. It is absolutely necessary, however, first to find the connection of the axis-fibrillæ with larger medullated or non-medullated nerves before we can positively determine their nervous nature.

Recently, a number of formations in the organs of sense have been termed *Neuro-epithelia* (Schwalbe). This refers to formations which are either epithelia or take a genetic origin from epithelia, and represent the terminations of the sensual nerves. In this group are included the rods and cones in the retina of the eye, which are composed of a number of transverse disks; the outer portions of the rods during life show a bright red color, which, by its discoverer, Boll, was termed the "visual purple." The rod- and cone-fibers, with their nucleated nodules, constitute the external granular layer of the retina. In the labyrinth, or the internal ear, especially in the maculæ and

cristæ acousticæ, are found the ciliated auditory, and between these the non-ciliated, so-called indifferent epithelia. In Corti's organ within the cochlea there exist the so-called hair-epithelia, which are divided into the inner and outer, the latter being arranged in four continuous rows along the external pillars. In the gustatory buds (Schwalbe, Lovén) there are filiform bodies surrounded by covering epithelia; they are found on the epithelial investment of the circumvallate papillæ, on the epithelia of the hard and soft palate, and of the posterior surface of the epiglottis. In the olfactory region of the mucosa of the nasal cavity, Max Schultze discovered, in addition to large, columnar, non-ciliated epithelia, interposed delicate nucleated filaments, which, in amphibia and birds, but not in man, have delicate cilia at their external ends. In none of the formations of neuro-epithelium is the termination of the nerve-fibrillæ clearly elucidated.

Pigmented Epithelia and Endothelia in man are of infrequent occurrence, while in the lower animals they are exceedingly abundant. The pigmented epithelial layer of the human retina is composed of very regular, hexagonal, flat bodies, the central nucleus, as well as the cement-substance, always being without pigment. The amount of the pigment, and also its shade, varies greatly according to the general complexion of the individual. The more blonde this is, the less pigment will be found in the epithelia, and in albinotic persons it is entirely absent. From the inner surface of the epithelial bodies numerous filaments arise, passing between the rods. These filaments are slightly pigmented in man, but in birds, fishes, and amphibia they abound in coloring matter.

Glands. All the organs of the body properly termed glands are formations of the epithelium. Some authors have given these epithelia the unnecessary name of "parenchyma or enchyma cells." The large majority of glands are composed of a single layer of epithelia. In the body of the gland the cuboidal variety is usually found, and in the duct the columnar; the cuboidal, however, are sometimes so much elongated as to represent the short columnar variety. Several layers of cuboidal epithelia are seen in the sebaceous glands and the prostate of the adult.

We distinguish two varieties of glands—viz., the acinous and the tubular. (See Fig. 141.)

A roundish, pouch-like prolongation of the epithelial layer into the connective tissue forms a *simple acinous gland.* Examples of this variety are the mucous glands of the oral cavity, the larynx, the trachea, and some of the sebaceous glands. Repeated foldings of the pouch constitute the formations called *compound acinous or racemose glands,* such as the sebaceous, the lachrymal, the salivary, the lacteal, the prostatic, and other mucous glands —f. i., those in the mucosa of the tongue, of the duodenum, of the trachea, and the glands of Cowper and Bartholini. A third

variety is the *currant-shaped racemose gland*, in which the acini encircle the longitudinal duct, as in the Meybomian glands.

A prolongation of the epithelium in the longitudinal, or rather in a vertical, direction is termed a *simple tubular gland*, such as the pepsine, the intestinal, and the utricular glands. Repeated ramifications of the tubules result in the formation of *compound tubular glands;* for example, the uriniferous and seminiferous tubules. Another sub-variety of tubular glands may originate by the coiling of the tubule. Examples of these coiled tubular glands are the sweat and ceruminal glands.

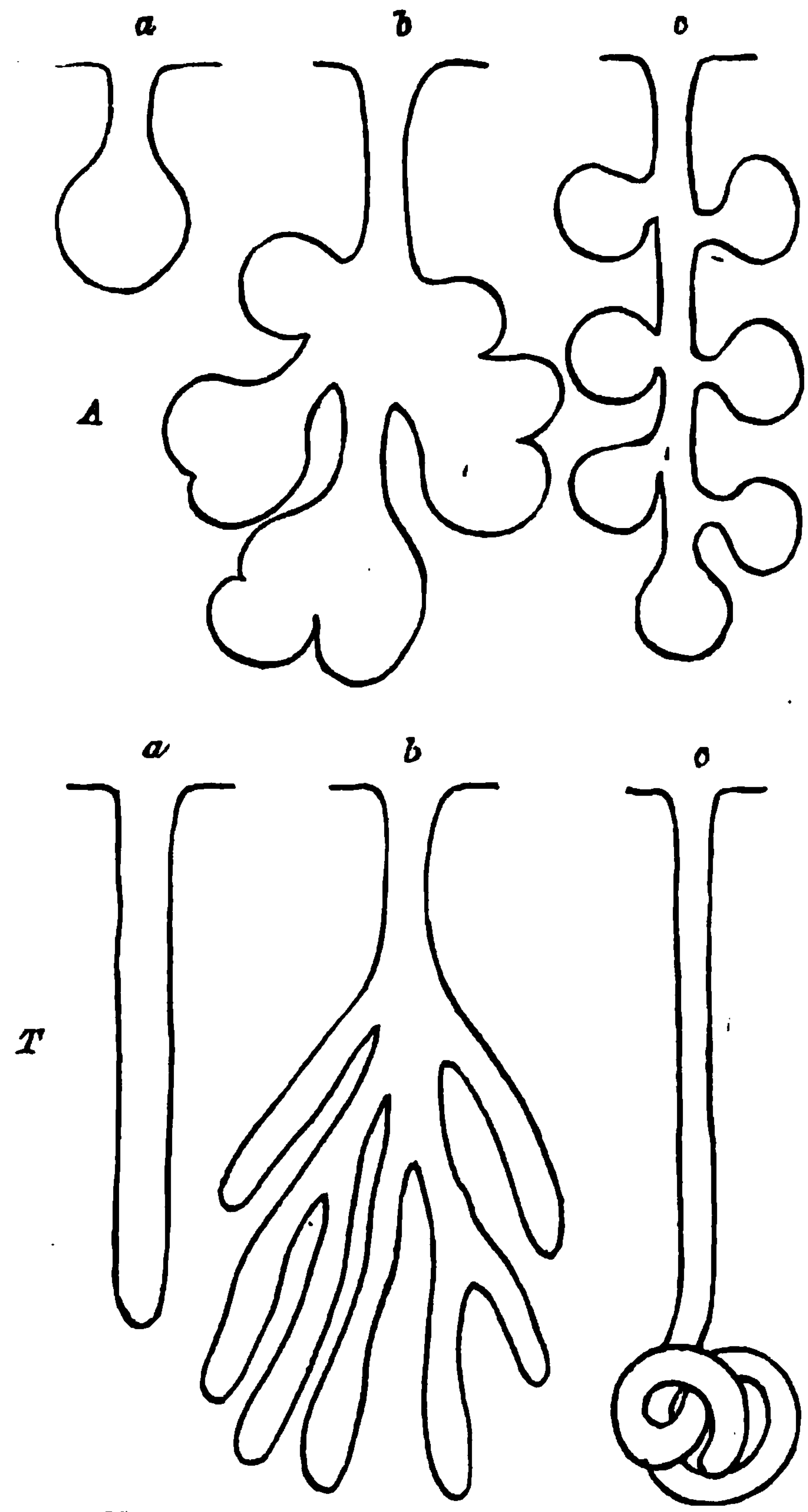


FIG. 141.—DIAGRAM OF GLANDS.

The series *A* exhibits the varieties of *acinous glands:* *a*, the simple pouch; *b*, the branching racemose form; *c*, the branching currant form.

The series *T* exhibits the varieties of *tubular glands:* *a*, the simple tube; *b*, the compound branching tube; *c*, the coiled tube.

There are transitions between these two principal varieties, when the acini are slightly elongated, as in the prostate, in the mucous, or Littre's glands of the urethra, and the mucous or Brunner's glands of the duodenum.

According to this definition, only epithelial—*i. e.*, secreting formations—can properly be designated glands, and all the so-called lymph-glands, the adenoid lymph-ganglia, the spleen, the thymus, and the thyroid body should be excluded from the glandular system, as they are not secreting, neither are they epithelial in structure.

The epithelia rest upon a delicate hyaline layer of connective tissue, which bears the superfluous name of a "membrana propria." It is of varying width, and is identical with the "base-

ment membrane" of Bowman. Between the epithelia and the hyaline layer a flat, delicate endothelial formation is often found, which is well marked in the seminiferous tubules (Mihalkovits) and in the uriniferous tubules (C. Ludwig). The hyaline layer of the salivary glands exhibits, according to Boll, delicate radiating spokes, emanating from the flat, central nucleus, which may be considered either stellate connective-tissue corpuscles, or rib-like ledges of the apparently structureless membrane. Outside of this layer is a delicate interstitial structure of fibrous connective tissue, freely supplied with blood-vessels and nerves. Connective tissue envelops the larger glands, forming a dense, firm capsule, called the tunica albuginea.

The nerves of the interstitial connective tissue are of both the medullated and non-medullated varieties, and not infrequently small ganglionic elements are met with along their course. The ultimate terminations of nerves are not yet fully understood; but, as far as my own observations go, I feel inclined to regard the termination represented in Fig. 140 as the most common.

Very little is known about the lymphatics of the glands. The so-called lymph-spaces, produced by parenchymatous injection, are unquestionably artificial formations, and are not entitled to the name of lymphatics. A complete system of lymph-vessels is known to exist in only the testes.

Performances of Epithelium. The principal function of epithelium, besides the *protection* of the body, the transmission of terminal nerve-fibers—therefore of *sensation*, etc., is the elimination of effete material from the body, viz.: by *secretion* and *excretion*. The horny, epidermal layer of the skin, on account of its indifference, within certain limits of course, to the action of acids and alkalies, and on account of its being a bad conductor of heat, serves for a protection to the body and all cavities exposed to the outer world. *The chief office performed by epithelia is unquestionably that of secretion*, which is carried on exclusively by epithelia, arranged as glands. Every glandular formation is epithelial, and each epithelial body may be looked upon as a gland, inasmuch as all secretory action is based upon the function of each single epithelium. All those processes which are considered the most disgusting in the animal economy are performed by epithelia; but it is epithelium, also, which produces the sweet, nourishing liquid called milk, and all its derivations, and which gives rise to the most essential material of generation—viz.: the spermatozoids and the ova.

Aside from some special secretions, *there are three varieties—viz.: the watery, the mucous, and the fatty.* (See Fig. 142.)

(a) The watery secretion cannot be directly studied under the microscope. We may infer, by watching amœbæ laden with carmine particles, that, at the time when, through the visible contraction of the living matter within the body, carmine particles are thrown out from the interior of the amœba, a certain amount of its fluid is discharged with them. We come to this conclusion from the fact that the carmine granules are extruded with a certain force, in a stream of liquid. We must also conclude that the opening in the wall of the amœba kindly and immediately closes, for the amœba displays the same amount of activity after

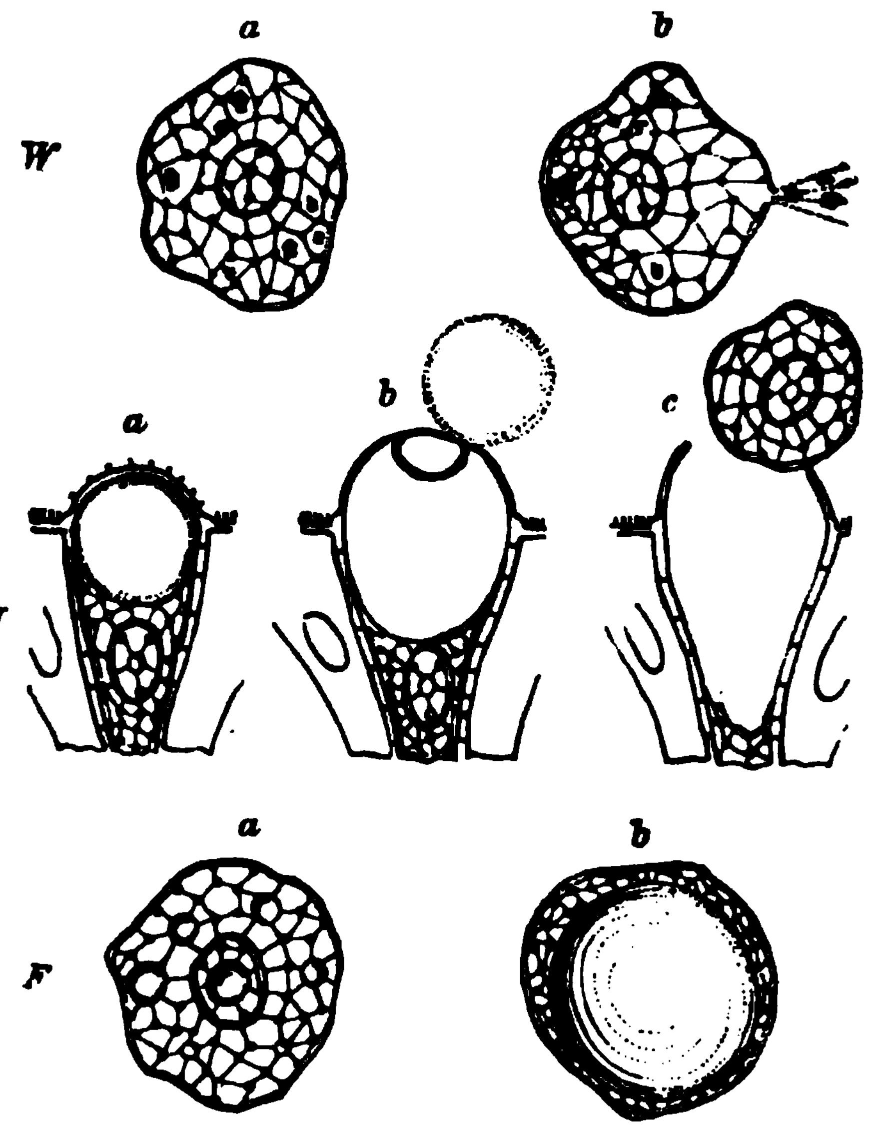


FIG. 142.—DIAGRAM OF THE PROCESS OF SECRETION.

The series *W* illustrates the *watery secretion: a*, a plastid, with foreign granules in meshes of the reticulum; *b*, escape of some granules, with some bioplasson liquid.

The series *M* illustrates the *mucous secretion: a*, mucous globule formed at the top of epithelium; *b*, a mucous globule discharged; *c*, a mucous corpuscle discharged; in both cases a goblet left.

The series *F* illustrates the *fatty secretion: a*, first-formed fat-granules; *b*, coalescence of fat-granules into a fat-globule.

as before this process. A liquid present in the blood, which to be excreted, must necessarily pass through the walls of th blood-vessels and first enter the epithelia before it can be expelle from them. The discharge of a certain amount of liqui

is evidently due to the contraction of the living net-work of the epithelium, on the one hand, and a rupture in the wall of the epithelium, on the other. This aperture probably closes immediately upon cessation of the contraction and reëstablishment of relative rest in the reticulum. Watery secretion is accomplished by the lachrymal and the sweat glands. The latter produce a fluid, varying greatly in the amount of its solid constituents and its consistency at different times, which indicates that the living matter of the epithelium itself has an influence on the chemical nature of the secretion. At the approach of death, the perspiration is inspissated and almost mucous in character. The main function of the uriniferous tubules is the inspissation of the fluid pressed out from the blood-vessels of the tufts of the kidneys.

(b) The mucous secretion can be directly observed under the microscope best on a minute particle, cut from the inner surface of the small intestine of a frog, with the addition of a very dilute solution of chromic acid or bichromate of potash; pure water acts with too much rapidity. We first observe a swelling of the body near the outer or free surface of the columnar epithelium. This can be accounted for by assuming that the epithelium imbibes the liquid which causes the swelling of the meshes of the bioplasson reticulum, and at the same time produces a considerable stretching of the reticulum. A contraction of the posterior portion of the bioplasson reticulum results, and this also assists in the enlargement of the anterior portion. The covering cement-substance of the free surface protrudes, and its delicate rods fall off. The cement-substance, after having reached its utmost capacity of expansion, bursts, and a pale, globular body is thrown out—*i. e.*, the swelled portion of the epithelium, in which no trace of the former structure can be seen. We must admit, however, the presence of a stretched reticulum in the mucous globule, too, and also an extremely thin, expanded, investing layer of the bioplasson. A number of the above described pale mucous globules coalesce and form the jelly-like mass called mucus.

When the process of swelling goes on more slowly, the whole bioplasson enlarges within its envelope of cement-substance, and after being freed, the nucleated plastid, now termed "mucous corpuscle," still exhibits the net-like structure; or we may see isolated, torn granules in an active, so-called "molecular" motion, the broken particles of the former bioplasson reticulum.

Salivary and mucous corpuscles arise by this same slow action from the contents of the epithelia. The investment of the cement-substance, being partly or totally emptied and perforated at one end, gives the appearance of a "goblet-cell." Formations termed goblet-cells are met with, in numbers greatly varying on all mucous surfaces; they are very numerous in the small intestine of rabbits suffering from diarrhœa, and also in the mucosa of the artificially inflamed stomach of animals (Stricker and Kocslakoff).

A similar process of the formation of mucus is often observed in the mucous glands of the frog's skin; here the production of

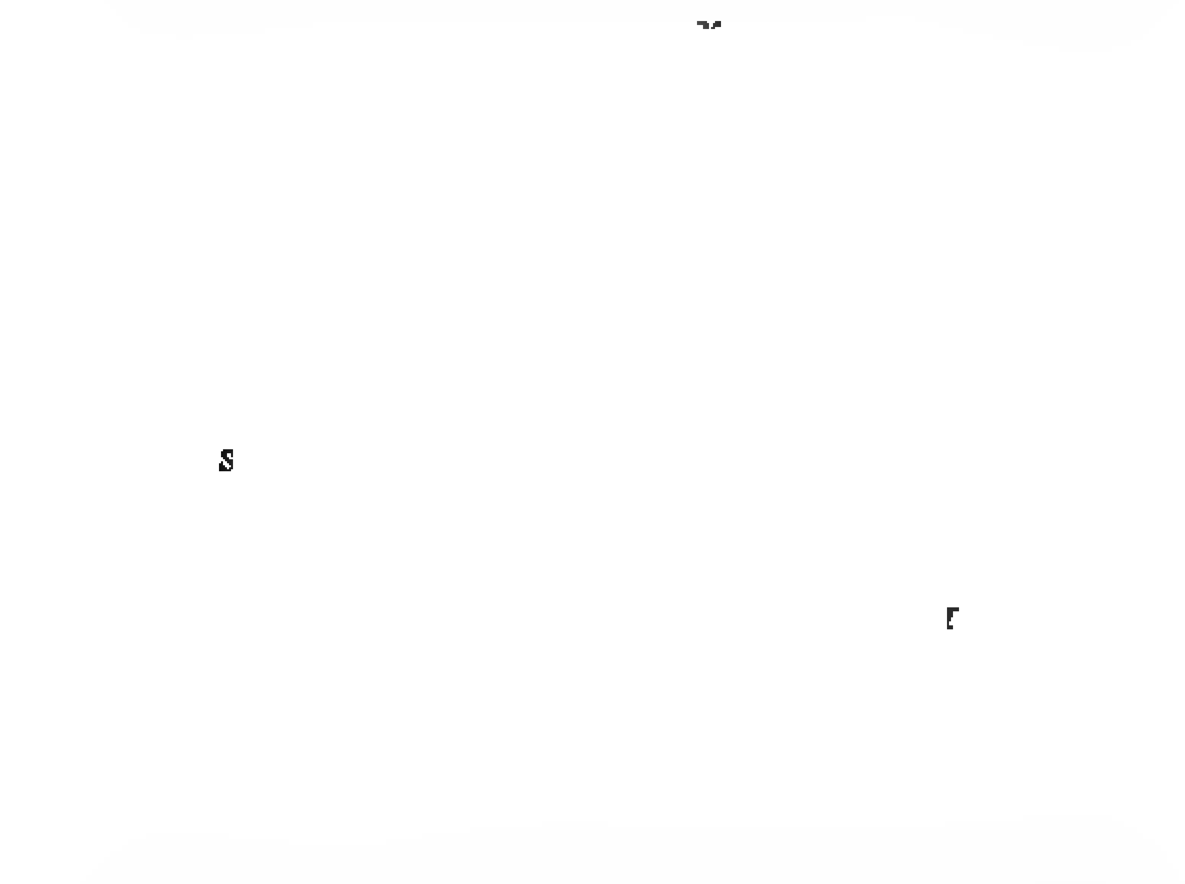


FIG. 143.—MUCOUS GLANDS FROM THE SKIN OF A FROG.

C, connective-tissue frame, carrying medullated nerve-fibers, *N*, coursing between the glands, *S*, and sending delicate ramules to the cement substance of the epithelia; *E*, elongated cuboidal epithelia, partly transformed into *M*, the mucous globules; *L*, the central caliber. Magnified 400 diameters.

mucus from the epithelia of the gland is diagrammatically plain. (See Fig. 143.)

A variety of mucous secretion is that of the *stomachic juice*, of the *bile*, and the *semen*. The acidity of the stomachic juice is unquestionably due to a peculiar chemical action of the living matter of the epithelia, for the blood is always alkaline. The bile is a product of the liver-epithelia, each of which is a labor-

atory, manufacturing chemical products from the plasma of the blood, and probably also from the red blood-corpuscles. The coloring matter of the bile is known to be closely allied to hæmoglobine. In the fluid of the semen formations of living matter are suspended—the spermatozoids, which are direct offsprings of the epithelia of the testicles. Saliva represents an intermediate condition between the watery and mucous secretions.

R. Heidenhain first drew attention to the differences in the aspect of the epithelia of the salivary glands, under the different conditions of fullness and contraction. He found the epithelia in starved dogs light colored, very much swelled, partly destitute of granules, and unaffected by the carmine stain, although the nucleus would be deeply colored. In epithelia of dogs, which before death were abundantly fed, or whose salivary glands, by means of electricity, were stimulated to an intense and long-continued secretion, the epithelia were, on the contrary, small, regular in outline, and their nuclei less stained with carmine. In the first case, the central caliber was imperceptible; in the latter, it was very distinct. The same observer discovered in the epithelia of the pancreas, also, peculiarities depending upon the state of the secretion. He called the upper portion of the epithelium granular, the lower light portion structureless; and in the process of secretion the upper layer predominated largely. Heidenhain and Rollett discovered varieties of epithelia in the pepsine glands, which were unlike in appearance, some being very large and swelled, with a distinct nucleus; others small, about the size of the ordinary cuboidal epithelia, and not distinctly nucleated. These facts, inexplicable to their discoverers and more recent investigators, are fully understood by recognizing the presence of the bioplasson reticulum of the epithelial bodies within the investing layer of cement-substance. When the epithelia of the salivary, the pancreatic, and the stomachic glands are laden with secretion, the meshes of the reticulum are enlarged, and the reticulum itself stretched; but when the epithelia are emptied of their secretion, the reticulum is in a condition of equilibrium. Bioplasson is accumulated in larger quantity at the portion of the epithelia, nearest to the connective tissue, exhibiting at all times a nearly homogeneous, shining appearance.

Unquestionably, in the process of mucous secretion a portion, or it may be the whole, of the bioplasson of individual epithelia is destroyed. With this fact before us we can readily

understand the weakening of the whole organism by diarrhœa, the relief afforded by drastics in certain diseases, etc.

(c) The fatty secretion can be best studied under the microscope in colostrum corpuscles, which are suspended in the serous discharge of the mammary glands for a few days after delivery. Here we see the first-formed fat-granules still in connection with the net-work of the living matter within the plastid, and we arrive at the conclusion that fat is a directly transformed living matter (see page 28). During the active locomotion of a colostrum corpuscle, very often fat-granules are thrown up from its interior (S. Stricker). After a few days, however, no more colostrum corpuscles are secreted, because the living matter of the epithelia is nearly completely transformed into fat-granules, leading to a continuous destruction of the epithelia, the granules of which commingle with a serous fluid and form the emulsion called *milk*. This process of fatty change in the living matter of the epithelia of the mammary glands is a remarkably rapid one. In microscopic specimens of a breast from the corpse of a nursing woman, we find in the secretory epithelia little unchanged bioplasson, the greater part of it being transformed into fat-granules. If these be extracted from the specimen with oil of cloves, only the shells of the cement-substance of many of the epithelia are left behind. Through what agencies the enormously augmented bioplasson becomes transformed into fat is at present not understood. There is no doubt, however, that this material is an offspring of the epithelia. Those who claim that the new material for the formation of milk are "leukocytes," or emigrated colorless blood-corpuscles, are in the dark regarding the nature and the function of epithelia and glands. The serous liquid in which the small fat-granules of the milk are suspended evidently comes from the blood-vessels; for it is well known that abundant drinking increases the quantity of milk. The amount of milk furnished by one udder, in the act of milking, greatly exceeds the volume of the udder, which indicates that a continuous flow of the plasma of blood takes place during the milking process. Toward the end of milking, the plasma being exhausted, very rich, inspissated milk is obtained.

The highest degree of fatty change of the bioplasson is reached in the sebaceous and the ceruminal glands. The wonderful apparatus for the extrusion of the fat from the sebaceous glands will be spoken of in the chapter on the skin.

THE VASCULAR SYSTEM.

The vascular system is formed from the middle germinal layer,—the mesoblast,—and especially of the connective tissue, which alone carries blood-vessels. The different portions of this system are the heart, the arteries, the capillaries, and the veins. In the heart the muscular apparatus is highly developed, as this is the principal motor for the blood current. Arteries always have a muscle coat, which is comparatively more developed the smaller the caliber of the vessel, evidently to admit of an independent activity in the motion and distribution of the blood. The veins have a thinner coat of muscular tissue than the arteries, while the capillaries have no muscular investment whatever. The layer constantly present in the heart, as well as in all blood-vessels, is the most internal—viz.: the endothelial. This, as previously mentioned, is the representative of the investment of living matter of the vacuoles, which are visible at times in single plastids. The endothelial layer, in the earliest stages of formation of blood-vessels, is a continuous investment around the vacuoles, and in a later stage of development divides to form single plastids, which, although separated from each other by a narrow rim of cement-substance, still remain interconnected throughout life by means of delicate filaments ("thorns"). The cement-substance, under certain conditions, becomes permeable to both colored and colorless blood-corpuscles. The nourishing material—the plasma of the blood—must necessarily penetrate the endothelial layer before it can reach the neighboring tissue, and the number of blood-vessels is always proportionate to the activity of the tissue in which they lie. Muscles—f. i., glands, the gray substance of the nerve-centers—are abundantly supplied with blood-vessels; while the comparatively inert cartilage, on the contrary, has a very limited supply. Blood-vessels are found in the greatest numbers in the organs in which the oxydation of the blood is accomplished—*i. e.*, the lungs. What influence the bioplasson of the endothelia has upon the exchange of liquids and gases we are unable to say; this much is certain, however, that all endothelia are bioplasson formations, manifesting vitality in a high degree, and not "elastic plates," as some histologists claim. The striking changes that occur in endothelia during inflammation are a direct proof of their life and activity.

(1) *The Heart.* The muscle of the heart is composed of branch-

ing and anastomosing striped fibers, with very small sarcous elements (see page 272, Fig. 116). The fibers are arranged in bundles and surrounded by a connective-tissue envelope,— the external perimysium,— which sends prolongations between each single muscle-fiber and its neighbors; this last formation constitutes the internal perimysium. The points of attachment for the muscular fibers of the heart are the fibrous rings at the auriculoventricular openings and the tendons of the papillary muscles. The perimysium is abundantly supplied with blood-vessels and lymphatics. Hyrtl discovered that the heart of many low vertebrates — f. i., the frog — is destitute of blood-vessels, and that sinuous prolongations from the cavities of the heart take their place. The endocardium and the pericardium have a capillary system with wide meshes. In reptiles and most of the fishes, according to the same observer, the muscle of the heart is composed of two distinctly separated layers — a broad inner, which is without blood-vessels, and a narrow outer, layer, which has a well-developed capillary system.

The *endocardium* is composed of a layer of fibrous connective tissue, varying in width in different portions and largely intermixed with elastic substance. The inner surface of this structure is covered by a delicate layer of large and flat endothelia, which is attached to a homogeneous, so-called hyaline membrane. The dense, fibrous connective-tissue partitions termed the valves, originating from the rings of the ostia, are also covered with endothelia. According to Gussenbauer, there are found in the peripheral portions of the valves, on the surfaces looking toward the auricles, numerous circular and radiating muscle-bundles, which come from the muscles of the septum of the auricles. The muscle layer of the auricles, however, is much less developed than that of the ventricles, while the elastic layer beneath the endothelia is very marked. In many places, the structure of the wall of the auricles is similar to that of the large arteries. Purkinje's filaments in the endocardium of cattle and other animals are considered as peculiar forms of development of striated muscle-fibers.

The *pericardium* is a connective-tissue formation, composed of coarse interlacing bundles in the parietal, and of delicate interlacing bundles in the visceral, portion. The free surface of both portions is covered with flat endothelia. The plexuses of blood-vessels and the lymphatics are broader in the pericardium and endocardium than in the muscle of the heart. According to

Wedl, the lymphatics are very numerous in the fat-tissue lying beneath the visceral layer of the pericardium.

The *nerves* of the heart are of both the medullated and non-medullated varieties. The former are branches of the vagus nerve, the latter of the sympathetic system; the plexus cardiacus is a combination of both. The subserous branches accompany the coronary vessels in plexiform arrangement, and are studded with ganglionic elements, single or in groups. The termination of the nerves in the muscle of the heart has not yet been demonstrated.

(2) *The Arteries.* Their walls are composed of at least three layers, the inner of which—the *intima*—is endothelium; the middle—the *media*—smooth muscle; and the outer—the *adventitia*—a connective-tissue formation. These three layers are very firmly connected with each other; the relative thickness of these coats varies greatly with the size and the location of the vessel. (See Fig. 144.)

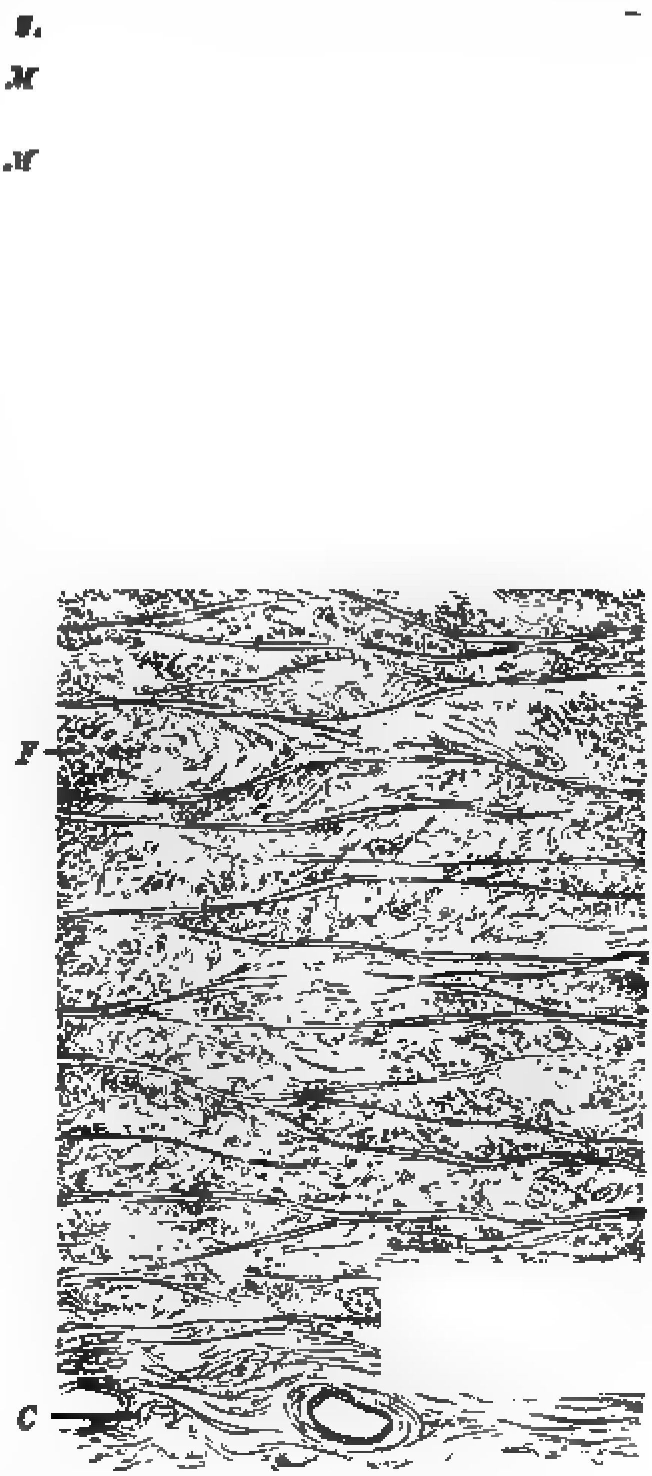


FIG. 144.—WALL OF THE EXTERNAL CAROTID OF MAN. TRANSVERSE SECTION.

E, endothelial layer, beneath which is a hyaline, so-called elastic, layer; *MM*, smooth muscle in longitudinal and transverse section; *F*, dense fibrous connective tissue, with a network of broad elastic fibers; *C*, loose connective tissue supplied with capillary blood-vessels. Magnified 200 diameters.

The *inner coat* is composed of flat, nucleated endothelia, exhibiting the usual bioplasson reticulum. These bodies are elongated in the longitudinal direction of the artery, and in edge view appear spindle-shaped, owing to their middle

broadest diameter at the seat of the nucleus. The separating cement-substance is best demonstrated by the injecting of gelatine, to which a two per cent. solution of nitrate of silver is added. Upon treatment with distilled water and exposure to daylight, the lines of the cement-substance appear dark brown in color and pierced by numerous tranverse light lines, which (see page 125) correspond to the connecting filaments of living matter ("thorns" or "prickles"). Not infrequently dark brown dots or delicate rings are visible along the brown line of the cement-substance, varying greatly in number in different localities; these are the so-called stigmata.

In the smallest arteries, the *arterioles*, there is an extremely delicate structureless membrane, next to the endothelia. The two together have a fluted contour, and the cement-substance a zig-zag appearance, evidently on account of the contraction of the middle or muscle coat. In larger arteries, the structureless membrane is found to be considerably broader and fenestrated —*i. e.*, with numerous, irregularly distributed perforations; in still larger arteries, the fenestrated membrane is replaced by a dense reticulum of elastic fibrillæ.

In the largest arteries two more or less distinct layers are found over the endothelium; the inner being the hyaline or elastic membrane proper, the outer a reticulum of elastic fibrillæ.

The *middle coat* is composed of smooth, spindle-shaped muscle-fibers, which in the terminal arterioles are present in one layer only, twined around the vessel. In longitudinal sections of arterioles, these fibers are easily recognized by their transverse sections along the wall outside the endothelium. The nucleus of the fusiform muscle-fiber, which is rod-like in front view, becomes visible in the transverse section only when the middle, broadest portion of the spindle shows its optical section. As the caliber of the artery enlarges, the muscle spindles become augmented, being very numerous in the larger arteries. Here, also, a longitudinal layer of muscle spindles becomes apparent, outside of the circular layer; but the longitudinal layer nowhere reaches a high degree of development. In the middle coat of larger arteries the bundles of smooth muscles are separated by elastic fibrillæ, and in the largest arteries by continuous membraneous formations of elastic substance, which attain their highest development in the aorta. In this situation the lamellæ usually take an oblique course, and are connected uninterruptedly with the elastic reticulum above and below the muscle coat.

According to C. Toldt, the muscle-fibers of the middle coat are wanting in the initial portion of the aorta, in the pulmonary artery, and in the small arterioles of the retina; in the aorta descendens, the A. iliaca communis, and the A. poplitea small muscle bundles, in an oblique or a longitudinal direction, are interspersed between the circular ones; and in other arteries (A. renalis, lienalis, spermatica interna), at the inner boundary of the muscle coat, scanty longitudinal bundles occur, which, by some authors, are considered to belong to the inner coat. Sometimes, in the corresponding arteries of different persons, slight differences are observed in the distribution of the muscles of the middle coat.

The outer coat is composed of fibrous connective tissue, which varies greatly, both in amount and density, in different vessels. In the smallest arterioles it is only slightly developed, while in the largest arteries it attains considerable breadth. In medium-sized arteries, the muscle layer toward the connective tissue is bounded by a hyaline, elastic membrane, which in the large arteries is widened into a thick layer of dense fibrous connective tissue. The bundles of this tissue are interlacing, and at their boundaries marked by a coarse, well-developed reticulum, or frame-work of elastic substance. This frame is denser in the neighborhood of the middle coat than toward the peripheral portion. The latter exhibits scattered bundles of smooth muscles in a longitudinal arrangement, and is gradually transformed into loose connective tissue, which composes the sheath of the artery, and carries a system of capillary blood-vessels, the so-called vasa vasorum.

The development of arteries was studied by J. B. Greene, who found that they are originally solid cords, composed of indifferent or embryonal elements. The most central ones become vacuoled; others are transformed into a flat layer to form the future endothelia; while the most external are elongated in shape, and assume a circular arrangement, this being the first trace of the future muscle-fibers. (See Art. on menstrual decidua.)

(3) *The Coats of Veins* are similar in composition to those of arteries; but the elastic substance and the muscle tissue is less developed in veins than in arteries. It is the middle coat, especially, which in veins varies most in breadth. This coat is also comparatively more developed in the veins of the lower than in those of the upper extremities. In the V. portæ, cava ascendens, and hepatica the muscle coat is only faintly defined, and its

bundles are separated by broad layers of fibrous connective tissue. A relatively large amount of muscle is found in the middle coat of the veins of the spermatic cord. (See Fig. 145.)

The muscle coat is almost completely wanting in the system of the V. cava descendens, in the veins of the nerve centers, and also in those of the bones. Here the middle coat is composed of delicate fibrous connective tissue, with more or less elastic fibers, running in a circular or oblique direction. The venous adventitial coat is likewise less developed than the arterial, but contains a comparatively greater number of longitudinal bundles of smooth muscle, so much so that in the V. portæ and V. renalis these bundles form an almost continuous layer. In the adventitial coat of the veins which empty into the heart, near their cardiac orifices, we find a varying amount of striated muscle-fibers,

TISSUE OF THE SPERMATIC CORD OF MAN.

A, artery, with *E*, endothelial and covering hyaline layer, *M*, smooth muscle layer; adventitial layer, *V*, vein, exhibiting the same layers as the artery, *C*,' capillary blo vessels, composed of a single endothelial layer, with a surrounding delicate advent fibrous connective tissue. Magnified 200 diameters.

The valves of the veins are reduplications of the inner co with a well-defined elastic reticulum, especially on the con surfaces, and with a complete endothelial investment.

The cavernous bodies are veins or sinuses of greatly varyi calibers, freely anastomosing with each other; they are sheathed by a dense connective-tissue capsule, which sen

numerous offshoots between the veins, and is in part freely supplied with smooth muscles.

Arteries and veins in specimens under the microscope may be distinguished from each other by the fact that arteries almost always are empty, or contain only a few blood-corpuscles, while veins, as a rule, hold a large amount of blood. Besides, the arteries are found to be contracted, their inner coat has a fluted, corrugated outline, while the veins are more or less smooth in their inner circumference. The wall of the artery is always broader than that of the vein, owing to the presence of the muscle coat, which, both in longitudinal and transverse sections, is well marked in the former and but slightly marked in the latter. In transverse sections of veins, also, transverse sections of the longitudinal muscle-fibers are often recognized. Another point of difference between an artery and a vein, should the latter have a marked muscle coat (see Fig. 145), is that the artery has a circular or slightly oblong caliber, while the vein has an oblong, irregular, compressed, or hour-glass shaped caliber. The adventitial coat, likewise, is decidedly thicker in arteries than in veins, though both may exhibit the nutrient capillary blood-vessels, the vasa vasorum.

(4) *The Capillaries* are composed of a single endothelial wall. Their plexiform arrangement is best brought into view by the injection of a stained, coagulating material. The density of the reticulum greatly varies in different parts and organs of the body. The closest reticulum is found in the lungs; the densest, and at the same time broadest, reticulum in the liver. In the latter organ, the caliber of the vessels show marked variations in size in comparatively small territories of the lobules; this is evidently due to a difference in the diameter of the liver epithelia in different stages of their activity. In the kidneys, too, there are striking differences in the calibers of the capillaries, some of which (the so-called vasa recta) attain the size of veins.

S. Stricker was the first to point out the fact that the wall of the capillaries is endowed with vital properties, and especially with that of contractility. Before him, the capillary walls were considered to be only an elastic membrane. Nobody can doubt, who has carefully observed capillaries in different situations, that during life the endothelial wall exhibits marked changes, according to its state of contraction, to the functional activity of an organ, and to the age of the individual. The injection of a colored material from without renders these differences, as a

matter of course, to a great extent imperceptible. Capillary blood-vessels are by no means permanent formations, but, according to the necessity of their vital activity, they are produced and destroyed—*i. e.*, transformed into the connective tissue from which they have originally sprung. That, with advancing age, a number of capillaries are transformed into bone, I have demonstrated (see page 236), and similar instances are found in all varieties of connective tissue.

All capillaries are surrounded by a delicate light rim, which is traversed by minute spokes of bioplasson, interconnecting the wall of the capillary with the adjacent tissue. This perivascular space, which certainly contains a liquid, was erroneously termed a lymph-space, because colored liquids can be forced into it from without by parenchymatous injection. Similar spaces, however, exist around all bioplasson formations and around the territories of connective tissue (see page 132), but they bear no relation to the lymphatic system. It will be seen that successful injections have demonstrated the presence, in the lymph capillaries, of an endothelial wall, similar to that of the blood capillaries. As both are permeable to the liquid and solid constituents of the blood and lymph, the assumption of an ensheathing lymphatic system around the blood-vessels is quite superfluous. Around the capillary blood-vessels which lie close to the arteries and veins there is often found a continuous layer of connective tissue, the so-called capillary adventitial coat. A distinct coat of this kind is found around all capillaries of the central nervous system (His). According to Boll there is no reason for terming this investing sheath, which is rendered very plain by parenchymatous injection, a lymph-sheath.

In the vicinity of capillaries, especially in the loose connective tissue, large, coarsely granular plastids are often found, the "plasma-cells" of Waldeyer, the significance of which is not yet fully understood. Here, however, is the place of the most intense nutrition, where the first and most prominent changes occur in the process of inflammation.

Upon being injected with a solution of nitrate of silver, the capillaries exhibit in many localities an elongated frame of brown cement-substance, with a varying number of stomata and stigmata. The flat endothelia, being broadest in their middle portion, where the nucleus is located, exhibit a spindle-shape both in longitudinal and transverse sections of capillaries. In numerous cases, however, no endothelium is rendered visible, even with the

silver staining, and the capillary appears as a continuous layer of bioplasson, which here and there is slightly thickened. This becomes comprehensible through the facts taught by the history of development of the capillary blood-vessels.

Nerves have often been demonstrated in the walls of capillaries by means of gold-staining. They appear as a delicate, beaded reticulum, running in the cement-substance, in the same manner as in epithelia. (See page 324, Fig. 140.)

Peculiar vascular formations are the *coccygeal* and *carotid "glands,"* and the *plexus choroidei*. They are composed of convolutions of capillary blood-vessels, with vesicular club-shaped or semi-globular prolongations, in connection with the caliber of the capillary. Neither the coccygeal nor the carotid gland are epithelial or glandular formations, therefore the word "gland" is a misnomer in this connection. C. Langer discovered in the mucosa of the palate and throat of frogs semi-globular prolongations of the capillaries, often with anastomosing the caliber of the capillary by means of a narrow pedicle. He considers these formations equivalent to capillary loops.

Development of Capillaries. S. Stricker (1865) first proved that the capillaries are originally solid strings, either connected with the wall of an already formed capillary, or representing solid, club-like outgrowths from this wall. These solid strings become afterward excavated, vacuoled, and the originally solid wall of the capillary is differentiated finally into endothelia.

My own researches corroborate this discovery of Stricker. I have seen solid, club-shaped formations in the middle of a medullary space, which were new formations produced by the retrogression of cartilage tissue to its embryonal condition. (See page 246.) I also have observed that the originally solid club or cord-like formations become vacuoled even before a connection is established with older blood-vessels, and that in the vacuole unchanged masses of bioplasson remain, which I have called hæmatoblasts, because they are the future blood-corpuscles. I made similar observations in the study of the process of inflammation in different varieties of connective tissue, all of which go to prove that a capillary is originally a solid mass of bioplasson, which by vacuolation becomes hollowed, while some particles of bioplasson are furnished with hæmoglobin, and converted into colored blood-corpuscles. In 1873, I said that wherever a transformation of one tissue into another takes place, either as a normal process, or as the result of inflammation, a new formation of blood-vessels and blood-corpuscles invariably occurs as a part of the process. The wall of the newly formed capillary is

at first solid—in other words, the bioplasson is in the juvenile condition. Later, the solid bioplasson divides into a reticulum, with, in the center, solid masses, termed nuclei. At the periphery the cement-substance is formed, though this, owing to the presence of the connecting filaments ("thorns"), never completely separates the single endothelia into individual cells. Thus, the wall of the capillary, even after the formation of endothelia, remains a continuous layer of bioplasson, endowed with contractility and with the capacity of growing, especially in the inflammatory process. In retrogression of the capillaries the hollow bioplasson is first solidified, then breaks up into medullary elements and gives rise to connective tissue, from which, under all circumstances, the capillaries have originated.

Th. Schwann * found in the germ-membrane of the ovum of the chicken, thirty-six hours after hatching, cells which, by elongation in different directions, became stellate. He called these cells the cells of capillary vessels, and considered the blood-corpuscles as young cells formed in the cavity of the capillary vessel cells.

C. Rokitansky † knew that in certain morbid processes, especially in the growth of cancer, blood originates in cells which had become tubular or club-shaped. The prolongation of the cells he considered as a beginning new formation of blood-vessels. He also maintained that a so-called insular new formation of blood took place in the process of inflammation.

S. Stricker ‡ asserted that the capillary tube is a hollowed out protoplasma endowed with many of the characteristics of life; that a solid thread, first simply an offshoot of a capillary vessel, afterward becomes hollow; that in the tail of the tadpole there are vessels filled with colored blood-corpuscles, terminating at either end in the shape of extremely delicate solid processes.

E. Klein § demonstrated that in the germinal disk of the chicken embryo, in the first half of the second day of hatching, some elements of the middle germinal layer exhibit vacuoles. These vacuoles, he asserted, were the first formations of blood-vessels, and that from its protoplasmic walls masses are separated, partly colored and partly colorless—the blood-corpuscles. In other cells of the same germinal layer, occasionally multinuclear, he observed in the center an endogenous formation of blood-corpuscles, while the periphery of the cell was transformed into the endothelial wall of the vessel.

My own researches ‖ have resulted in the conclusion that living protoplasma, in the condition termed "hæmatoblastic,"—viz.: in a juvenile condition of development,—is the material from which originate both the colored blood-corpuscles and the wall of the blood-vessels.

* "Mikroskopische Untersuchungen," etc., 1839.

† "Handbuch der Allg. Patholog. Anatomie," 1846.

‡ "Studien über den Bau und das Leben der capillaren Blutgefässe." Sitzungsber. d. Wiener Akad. d. Wissensch., 1865.

§ "Das mittlere Keimblatt in seinen Beziehungen zur Entwicklung der ersten Blutgefässe u. Blutkörperchen im Hühnerembryo." Sitzungsber. d. Wiener Akad. d. Wissensch., 1871.

‖ "Ueber die Rück-u. Neubildung von Blutgefässen im Knochen u. Knorpel." Wiener Mediz. Jahrbücher, 1873.

THE LYMPHATIC SYSTEM.

During the last fifteen years many erroneous views concerning the lymphatic system have arisen, due to the method of studying—viz.: by "parenchymatous injection" of colored liquids. Perforations were made at random into the tissues of the body, and liquids were then forced in from without. The results and views obtained by this means are only worthy of being forgotten. On the other hand, careful injections of the lymphatics themselves, by Teichmann, Langer, Sappey, and others, have shown conclusively that the system of lymphatics is a closed one, just as that of blood-vessels. Throughout the lymph-ganglia, the spleen, and the lymph tissue in general, erroneously termed "adenoid tissue," lymph-vessels probably do not exist. The difficulties in rendering the lymphatics distinct by injection are very great, on account of the delicacy and transparency of their walls, their colorless contents, and the presence of valves arranged in the same manner as in veins.

The *lymph-vessels* form a reticulum, in the average wider than that of the blood-vessels, exhibiting in its peripheral ramifications, besides loops, pointed or club-shaped terminations. Lymph-vessels are characterized by irregular excavations and sinuses, and run either parallel with the blood-capillaries or independently of them. They are, like the blood-vessels, found only in connective-tissue formations. The walls of the lymph-capillaries are composed of a single endothelial layer, whose elements, as a rule, are larger than those of the blood-vessels. Often, there is no other investment to be seen, and the lymph-capillaries in this case have the appearance of being channeled in and supported by the adjacent tissues. The lymph-capillaries are destitute of valves; but the collecting ramules are always found to possess valves which produce constrictions of the vessel, while close above the valve, in the more central portion, there is a widening of the caliber. The ramules accompany the arteries, often in the shape of a reticulum, which is also found around the veins, though less developed. The larger ramules exhibit a delicate investing elastic layer immediately above the endothelia, and with the increase of the caliber of the lymph-vessel this investment assumes a fibrous structure, and is supplied with smooth muscle-fibers. A distinct stratification of the wall is apparent only on those lymph-vessels which, in the extended condition, have a diameter of 0.8 to 1 mm. (C. Toldt). Here, three layers are

discernible, analogous to those of blood-vessels: the most internal is the endothelial, with an underlying delicate connective tissue, which, as a rule, holds a number of elastic fibrillæ; the middle coat is composed of circular smooth muscles, inside of which are sometimes found longitudinal fibers, and the outer layer is fibrous connective tissue, with interspersed bundles of smooth muscle-fibers. The reticulum of elastic fibrillæ constitutes a comparatively broad layer in the walls of the thoracic duct; here, also, the oblique muscle bundles of the adventitial coat are most distinctly marked.

In the lower vertebrates the lymph-vessels are often found dilated into lymph-sinuses, which, in part, are under the control of muscles—"lymph-hearts" (J. Müller). Many of the lymph-sinuses empty directly into larger veins. In mammals, such lymph-sinuses are of doubtful occurrence, though it is generally held that the lymph-follicles in the small intestine of rabbits are surrounded by such sinuses.

Von Recklinghausen discovered that the peritoneal cavity is in direct communication with the lymphatic system at the tendinous portion of the diaphragma. The peritoneum is expanded over the large lymph-vessels of this portion, being lined by comparatively small endothelia, the cement-substance of which is more or less closely perforated with minute openings, the stomata and stigmata. The nuclei of the endothelia are arranged in the form of a wreath around the stomata, and larger stomata are again surrounded by a wreath of very small, regular endothelia. Through these openings dissolved or finely granular colored substances, if injected into the peritoneal cavity, are carried directly into the lymphatics of the diaphragm (C. Ludwig, Schweigger-Seidel).

The method of Ludwig and Schweigger-Seidel ("Arbeiten aus der Physiologischen Anstalt zu Leipzig," 1867) is as follows: The abdominal cavity of a rabbit which was bled to death is opened; the V. cava, the aorta, and the œsophagus are tied to the vertebral column by means of a common ligature, and the corpse of the rabbit is divided into halves by an incision made below the diaphragma. The upper half is suspended, the head downward, in such a manner that the diaphragm assumes a goblet shape. A certain amount of water, holding dissolved Prussian blue, is poured in this goblet, and by artificial respiratory movement the diaphragm is carried up and down for several minutes. Next the peritoneal surface of the diaphragm is washed, and alcohol poured over it, in order to render the Prussian blue insoluble and fix the tissues. After excision, the center of the peritoneal surface shows white tendinous tracts bounding blue tracts. These latter are the larger lymphatics,

and the above-named observers considered them clefts between the tendinous bundles. On the pleural surface is observed a reticulum of lymphatics, which is blued by injection, the small vessels gradually passing into larger lymph-vessels. The colored liquid has penetrated the lymphatics through openings in the central portion of the peritoneum covering the diaphragm. The stomata present in this situation, and which are surrounded by small globular elements, were termed lymph-wells by Ranvier.

Dybkowski found similar openings also in the endothelial investment of the parietal pleura; these openings are confined exclusively to the intercostal spaces, while in the pleura covering the ribs the stomata are absent. By the injection of colored substances into the pleural sac, results are obtained similar to those in the peritoneal cavity. The subjacent lymph-vessels in all these localities are distinctly marked by an endothelium, therefore are not simply interstitial tissue-clefts. The assertion of Von Recklinghausen that the connective tissue is pervaded by spaces and canals, destitute of walls of their own, and thought to be the roots of the lymphatic system, is erroneous, as proved in the chapter on connective tissue. Every space rendered visible by the staining with nitrate of silver contains a bioplasson body demonstrable by staining with chloride of gold. The apparent connections between the "juice-canals" of the connective tissue and the lymph-vessels proper, in specimens stained with nitrate of silver, although rarely seen, are explicable by the fact that neither the bioplasson bodies nor the lymph-vessels take up the silver stain. Observers agree, however, that at the periphery of the connective-tissue corpuscles and of the territories there are narrow spaces containing a liquid; but we are not justified by any facts in connecting these spaces with the lymphatic system.

Lymph-ganglia and Lymph-tissue. These are peculiar formations of the myxomatous connective tissue, which are closely allied to the lymphatic system. Their characteristic feature is a delicate reticulum, the meshes of which are crowded with lymph-corpuscles—*i. e.*, bioplasson bodies exhibiting all stages of development, from a small, homogeneous granule to a nucleated plastid, similar to the colorless blood-corpuscle (see page 105 and Fig. 31). This tissue is widely spread throughout the submucous layers, and reaches its highest development in the youngest individuals. It is arranged in conglomerated heaps—the so-called lymph-follicles—in the tonsils, the pharynx, the base of the tongue, the wall of the stomach, the submucous layer of the intestines, in the lymph-ganglia, along the lymph-vessels in

regular localities, in the thymus, and in the spleen. Probably the thyroid body and the suprarenal capsule likewise belong to this group. Single heaps of this lymph-tissue are termed lymph-follicles; compound formations of lymph-follicles bear the name of lymph-ganglia. In the spleen of man the lymph-follicles (Malpighian corpuscles) are elongated, and they are everywhere in close relation with the arteries and arterioles.

The lymph-follicles are, according to generally adopted views, the widened beds of the lymph-vessels and brought into connection with the lymph either by being surrounded by lymph-sinuses or by a dense reticulum of lymph-vessels, while the interior of the lymph-follicle is destitute of lymph-vessels. Every lymph-follicle, moreover, is encircled by a rich reticulum of blood-vessels, which send a comparatively small number of capillary loops into the interior of the follicle, these sometimes not reaching its central portion.

The lymph-ganglia are composed of more or less globular *lymph-follicles*, their prolongations, the *follicular cords* and the *interfollicular strings*, located between the two-named formations. The follicles and follicular cords abound in lymph-corpuscles, having a relatively delicate and scanty myxomatous reticulum, while in the interfollicular strings the myxomatous tissue is largely developed, and the lymph-corpuscles are less numerous. Besides, the interfollicular strings hold numerous blood-vessels, while the follicular formations exhibit a comparatively limited vascular supply. The interfollicular strings have also numerous lymph-vessels, while the follicles have none whatever. (See Fig. 146.)

The lymph-ganglion is inclosed by a dense fibrous connective-tissue capsule, whose outer parts blend with the surrounding loose connective tissue, which is supplied with a varying amount of fat. In the capsule, and in the coarser offshoots, bundles of smooth muscle-fibers are found, which in the lymph-ganglia of cattle form a continuous layer (Von Recklinghausen). The fibrous capsule sends prolongations into the depth of the follicle, which soon changes into a myxomatous reticulum. In the interfollicular strings the myxomatous tissue is well developed, has oblong nuclei on most of the intersecting points, and contains in its meshes comparatively few lymph-corpuscles.

The interfollicular strings ensheath the follicles, which, as a rule, are formations consisting of a large globular or pear-shaped mass of lymph-corpuscles, and are found at the periphery, the so-called *cortex of the ganglion*. The globular follicles

send prolongations—the follicular cords—into the middle portion, the so-called *medulla* of the ganglion, and here the follicular cords freely unite to form a coarse reticulum, which is more or less distinctly marked from the surrounding interfollicular strings. The portion of the lymph-ganglion giving exit to the lymph-vessels is characterized by a relatively compact formation of fibrous connective tissue, inclosing elongated, empty spaces. This is the so-called hilus-stroma of His. The connective-tissue trabeculæ are known to be the carriers of the lymph-vessels, which are in open communication with the lymph-spaces or sinuses around the follicles, and in the follicular cords. All these spaces are lined by a single endothelial layer, and they are

FIG. 146.—LYMPH-GANGLION. TRANSVERSE SECTION.

C, connective-tissue capsule, outside with fat-lobules, *FA*; *FO*, lymph-follicle; *FS*, follicular cord; *IF*, interfollicular string, with numerous blood-vessels. Magnified 100 diameters.

also in direct connection with the meshes of the myxomatous reticulum. An endothelial investment has been found only on the larger trabeculæ of the myxomatous reticulum. The meshes of the reticulum of the interfollicular strings contain comparatively few lymph-corpuscles, while the meshes of the extremely delicate reticulum of the follicles and the follicular cords are crowded with them.

Two or more afferent lymph-vessels enter the ganglion on one pole and divide into a number of branches, the endothelium

of which furnishes the investment for the lymph-sinuses. The sinuses unite to form what Toldt calls the "terminal sinuses." From these sinuses two or more efferent vessels arise, which by anastomoses gradually decrease in number.

The arteries penetrate the lymph-ganglion both at the periphery and at the hilus. Their ramules occupy the middle of the interfollicular strings; these also contain a few capillary blood-vessels, all supplied with a distinct adventitial coat. The arterioles form a wide capillary net-work, traversing the follicles and follicular cords, and giving rise to the veins, which accompany the arteries. The capillary system of the follicles and follicular cords is, to a certain extent, independent of the capillaries of the interfollicular strings. The capillaries of the lymph-ganglia are easily permeable to colored liquids injected into the artery. The reasons for this have not been fully explained.

The *thymus body* is a lymph-ganglion belonging especially to fœtal life. It reaches its highest state of development during the first two years, remaining stationary up to the tenth year, and at the time of puberty it has almost entirely lost its follicular structure. The delicate fibrous investment of the thymus body sends numerous prolongations into the interior, giving to it a more or less lobular appearance. The follicular formations are less distinct in the thymus than in other lymph-ganglia, and are more closely aggregated at the periphery of a lobule than in its center. Numerous small arteries enter the thymus body at its periphery; a few larger ones at its posterior portion. The course which the lymphatics take in the interior of the thymus is unknown. In the period of its involution peculiar concentrically striated corpuscles (Hassal) make their appearance, kindred to the amylaceous corpuscles of the brain. Apparently, these are developed from the walls of the capillaries, most probably from their endothelia.

The *thyroid body*, in the earliest periods of embryonal development, exhibits a glandular structure—*i. e.*, is composed of acini, lined by cuboidal epithelia; the acini are closed on all sides and no excretory duct can be discovered. This body, in all probability, is an elongation of the outer germ-layer—the epiblast. At the time of birth, the epithelial structure is often still preserved. Sooner or later, however, the epithelia are transformed into indifferent or embryonal corpuscles, exhibiting the characteristics of lymph-corpuscles. We meet with small, homogeneous globules, and also with larger ones of the size and the structure of nuclei,

and still larger ones, representing globular, nucleated plastids. Simultaneously with this recurrence of the embryonal condition, even in children, many of the lymph-corpuscles perish and are transformed into a homogeneous, viscid, so-called colloid substance, which, in thyroid bodies of adults, is almost invariably found in the closed spaces, now termed alveoli. The lymph-corpuscles are often arranged in the shape of a wreath along the wall of the alveolus, and irregular clusters of these corpuscles are found scattered throughout the colloid mass. The stages of transformation of the plastids into the colloid substance can easily be traced. (See Fig. 147.)

FIG. 147.—THYROID BODY OF ADULT.

F, connective-tissue frame, carrying numerous blood-vessels; *L*, lymph-corpuscles; *C*, colloid mass. Magnified 500 diameters.

The connective-tissue capsule of the thyroid body sends numerous prolongations into its depths, which constitute the walls of the alveoli. A striking feature of this formation is the great number of blood-vessels and lymphatics which penetrate its interior. The significance of this body is, however, not understood.

The *suprarenal capsule* is composed of two layers — a cortical and a medullary layer. In the former we see radiating rows of polyhedral bodies, having the appearance of epithelia, which often contain fat-granules. The connective tissue throughout this body is an offspring of the outer capsule, and is seen between the rows of the polyhedral bodies; near the boundary line of the cortical layer it forms a delicate reticulum, characterized by a

varying amount of a brown, granular pigment. The myxomatous reticulum in the medullary portion contains in its meshes lymph-corpuscles varying greatly in size. Both in the medulla and the connective-tissue capsule there are numerous ganglionic nerve elements (Von Brunn) which are in connection with the sympathetic nerve, branches of which, in large number, penetrate the suprarenal capsule. This organ has likewise a large supply of blood-vessels. Its development and functions are still physiological puzzles.

The *spleen*, in its structure, is closely allied to the lymph-ganglia, though its relation to the lymphatic system is by no means clear. Like the lymph-ganglia, the spleen has also a connective-tissue capsule sending numerous offshoots into the depths of the organ, where it produces a delicate myxomatous reticulum. The meshes of this reticulum contain a comparatively small amount of lymph-corpuscles, while these form larger globular heaps, similar to the follicles of the lymph-ganglia,—the so-called Malpighian corpuscles,—and elongated tracts, similar to the follicular cords—the so-called pulp-cords. The connective-tissue capsule has for its outer investment the endothelia of the peritoneum; in many mammals it contains a large number of bundles of smooth muscles, which also pervade the mass of the spleen. In man, the number of fibers of smooth muscle in this organ varies greatly, although small bundles are unquestionably found in many cases. The connective-tissue septa of the spleen are in union with the outer capsule, and produce branching and anastomosing trabeculæ throughout the pulp. These trabeculæ carry the arteries and veins, both of which enter or leave the spleen at different points, usually far apart.

The arterioles in most mammals show a distinct adventitial coat, which is crowded in its whole extent with lymph-corpuscles, so much so that each pulp-cord is pierced in its center by an arteriole. In man, the lymph-corpuscles around the arteriole are accumulated in lymph-follicles, varying in size, and either uniformly surrounding the vessel or attached more or less eccentrically to one side of the vessel. A favorite seat of these so-called Malpighian corpuscles is the point of ramification of the arteriole. In mammals' spleens which abound in muscles,—f. i., in the badger's spleen,—we observe bundles of smooth muscle-fibers accompanying the artery and surrounding the follicle, which is in connection with the layer of lymph-corpuscles in the adventitia of the artery. (See Fig. 148.)

The myxomatous reticulum of the pulp-cords of the spleen contains in its meshes lymph-corpuscles in different stages of development and multinuclear bioplasson masses; also a varying number of pigment granules, either scattered in the lymph-corpuscles or grouped in the shape of dark brown pigment clusters. In accordance with the view that red blood-corpuscles originate in lymph-corpuscles, almost all observers describe lymph-corpuscles as containing colored blood-corpuscles; others maintain the origin of these corpuscles from the endothelia. Such views, however, are erroneous, and Johnstone has demonstrated the

FIG. 148.—FOLLICLE OF THE SPLEEN OF A BADGER, IN CONNECTION WITH AN ARTERY.

L, lymph-follicle; *A*, artery, penetrating the follicle. *Ad*, adventitial coat of the artery, crowded with lymph-corpuscles; *M*, muscle-strings of the spleen, accompanying the artery; *V*, blood- and lymph-vessels in transverse section; *P*, clusters of pigment in the tissue of the spleen. Magnified 500 diameters.

source from which the colored blood-corpuscles arise, both in the lymph-ganglia and in the spleen—here, especially, in large numbers. (See page 105.) The significance of the multinuclear bodies is unknown, and there is no reason to term them the graves of the colored blood-corpuscles.

The arteries send numerous branches into the adventitial lymph-tissue and the lymph-follicles; they finally divide into

terminal branches, which produce delicate capillaries for the supply of the connective-tissue septa and for the pulp-cords. The veins arise from these capillaries, and represent vessels with thin endothelial walls, susceptible of a high degree of dilatation (Billroth). These vessels traverse the interstices between the pulp-cords and the connective-tissue trabeculæ, and produce tassel-like formations, which finally collect into larger veins. A number of observers maintain that the arterial capillaries are directly connected with the capillary veins; that therefore the vascular system of the spleen is closed everywhere. Wedl even admits a direct communication between arteries and veins. Others believe in the presence of lacunæ, destitute of walls of their own, interposed between the terminating capillaries of the arteries and the roots of the veins. The latter view is not sufficiently supported, for the walls of the capillaries of the spleen, as well as those of lymph-ganglia, are easily permeable to stained liquids injected from without. The important question as to the termination and origin of the capillaries is unsettled.

The origin of the lymph-vessels is also a much-discussed question. Tomsa considers the lacunæ as the roots of the lymphatics, because he succeeded in injecting them through the lymphatics. Probably the relations are the same as in the lymph-ganglia. Besides the lymphatics of the pulp, there are others in the capsule, and Wedl found in the spleen of the horse and the sheep two layers, the superficial being composed of narrow capillaries and wide meshes, the deeper of large, sinus-like capillaries, freely anastomosing with each other.

The manner in which nerves terminate in the lymph-ganglia and in the spleen is unknown.

I have thus briefly presented the views of other observers, because, on account of the lack of personal researches, I have no positive knowledge concerning the structure of the lymph-ganglia and the spleen.

XI.

INFLAMMATION.

HISTORICAL SKETCH. The clinical features of inflammation have been well studied ever since Hippocrates's time, but the interpretations of its appearances under the microscope have passed through varying phases during the last forty years. The views regarding the nature of the inflammatory process have undergone changes corresponding with the advanced knowledge of biological facts. Two main conceptions of this process have controlled the observations made by means of the microscope—viz., the theories of humoral and cellular pathology.

C. Rokitansky,* the founder of the humoral pathology, originally considered inflammation to be a disturbance in the vascular system, a disease of the blood, whose mixture, the "krasis," gave a typical character to the nature of the inflammatory process. The greatest stress was laid on the *exudation*, a liquid coming from the blood-vessels, therefore a modified plasma of the blood. The favorite experiment at that time was the production of an artificial inflammation in the web-membrane of the frog. This apparently showed all the phenomena of inflammation. The membrane of a living frog, carefully extended over a cork ring and held in position by pins, exhibited distinctly and beautifully the blood-vessels and the current of the blood, marked by the rushing blood-corpuscles. Upon applying an irritating agent to the web, usually a drop of concentrated liquor ammoniæ, striking changes occurred in the current of the blood: first, an irregularity in the current, an undulation; next, a slowing, and, finally, a stoppage of the current in the irritated vascular districts. This "stasis" was considered the essential phenomenon of the inflammatory process. Simultaneously an inundation and swelling of the surrounding tissue was observed, owing to the exudation. All the newly appearing corpuscles, including both the inflammatory and the pus corpuscles, were termed exudation corpuscles, and, in accordance with the cell-theory established by Schwann, were thought to have originated from the exuded plasma of the blood, in a manner termed primordial genera-

* "Handbuch der Allgemeinen Pathologischen Anatomie," Wien, 1846.

tion (Urzeugung), which means a new formation of cells from a liquid containing no cells.

The reason for the dilatation of the capillaries, observed in the stage of stasis of the blood-current, was at that time a question much discussed, but never satisfactorily answered. Brücke's view — that the capillaries, after a few intense contractions, became paralyzed — was accepted as the most probable. The newly formed cells of the effusion, according to the theory of humoral pathology, gave rise to new tissues as well as to the formation of pus. The exudate itself was thought to become organized, and to produce pseudo-membranes or hypertrophy of the inflamed tissues.

C. Rokitansky* afterward changed his views concerning the origin of the inflammatory new formation. This great observer announced, in contradiction to the views of Virchow, that, in inflammation, proliferation comes not only from "connective-tissue cells," but also from "intercellular substances"; that the latter also increase and give rise to new formations. It will be shown later that this view, at that time not understood, is entirely correct, and that since 1873 we have obtained facts which establish it on a firm foundation. The theory of humoral pathology was shaken by R. Virchow.† This investigator asserted that the blood-vessels take but little part in the inflammatory process. He based his conclusions upon observations made by His in the inflamed cornea, and the observations of Redfern in inflamed cartilage, both tissues having no blood-vessels, yet becoming greatly changed by inflammation. The only active parts of the connective tissue, according to Virchow, are the cells, which, after attracting the exudation from the blood-vessels, being over-nourished, enlarge, divide, and subdivide, and finally give rise to the inflammatory new formation, from which originates new formation of connective tissue, hyperplasia, as well as pus. The theory that cells arise from a plasma was no longer maintained. Virchow held that an exudation could never organize a tissue, and that all new cells must necessarily be the offspring of former cells. The new formation of cells, according to Virchow,‡ starts from the nucleus, which is first divided, and the "cell-body" is afterward split up into new cells.

The cellular pathology was based on these fundamental assertions of Virchow, and it is certain that the great progress made in biological knowledge in our day originated from these views, which gradually became the leading ones, and are so even at the present time. That the cellular pathological views are, however, not fully correct, I shall endeavor to demonstrate later.

J. Cohnheim,§ in 1869, announced a new theory regarding the inflammatory process, founded upon the fact that in the exposed mesentery of the frog an emigration of colorless blood-corpuscles takes place from the capillary blood-vessels and the smallest veins. The history of the theory of the emigration of blood-corpuscles from blood-vessels is briefly as follows:

Waller,‖ in 1846, was the first who maintained having actually observed

* "Ueber das Auswachsen der Bindegewebssubstanzen u. die Beziehung desselben zur Entzündung." Sitzungsber. d. Wiener Akad. d. Wissensch., 1854.

† "Ueber Parenchymatöse Entzündung," Virchow's Archiv, Bd. iv., 1852.

‡ "Ueber die Theilung der Zellenkerne," Virchow's Archiv, Bd. xi. Cellularpathologie, 1871.

§ "Ueber das Verhalten der fixen Bindegewebskörperchen, bei der Entzündung." Virchow's Archiv, Bd. xlv.

‖ *Philosophical Magazin.* Two successive publications: 1846, I., p. 271 and 397; II., p. 398 *et seq.*

the emigration of colorless blood-corpuscles. According to his view, the wall of the blood-vessel in the exposed and expanded mesentery and the tongue of toads becomes perforated in the circumference of the corpuscle lying next to it, and the aperture in the wall left by the corpuscle is closed by the restorative power of the blood. That a real emigration takes place was a mere conclusion of his, and so was the assertion that the emigrated colorless blood-corpuscles were the mucus- and pus-corpuscles, which first appear along the walls of the blood-vessels.

S. Stricker,* in 1865, observed in tadpoles, immobilized by curara, colored blood-corpuscles, which were incarcerated in the wall of a capillary blood-vessel, so that a portion of the corpuscle was inside, another portion outside the capillary, and both portions were connected by a slender neck within the wall of the vessel. He concluded that the red blood-corpuscles could pass the wall of the vessel without a rupture, in a manner termed "*diapedesis*" by former pathologists.

J. Cohnheim,† in 1867, asserted that an emigration of colorless blood-corpuscles actually occurs, he having observed these bodies to pass through the wall of the vessel. He saw that the inner portion of the corpuscle decreased and the outer gradually increased in size, then that the corpuscle was attached to the wall by means of a thin pedicle, and finally detached entirely from the outer wall. Unfortunately, this observer came to the conclusion that the emigration of colorless blood-corpuscles is the principal factor in the process of inflammation, and that the entire mass of inflammatory corpuscles is nothing more than an aggregation of such emigrated corpuscles, while the tissue itself simply perishes, and its elements take no part whatever in the inflammatory process. A few authors have accepted this view of Cohnheim. They have spoken again of an organizing exudate, meaning the corpuscular elements of the blood, and had they but known whence came this enormous quantity of inflammatory corpuscles, the whole process of inflammation would have been very clear and simple to them.

S. Stricker‡ has, since 1870, strenuously opposed the views of Cohnheim. He demonstrated that each of the former theories contained some truth, and that from a combination the whole truth can be deduced. He proved the necessity of the presence of blood-vessels and nerves for the origin of inflammation, agreeing with the theory of the humoral pathologists, and showed that the connective-tissue cells themselves participate actively in the inflammatory process by swelling, dividing, and subdividing, in accordance with the views of the cellular pathologists. He was the first to prove the correctness of the hypothesis of John Hunter that the cells, and consequently the tissues, in inflammation return to a juvenile condition, in which the cells are enlarged, become amœboid and proliferate, while the "intercellular substance" is liquefied and destroyed. That an emigration of colorless blood-corpuscles really takes place in inflammation is a granted fact.

Stricker was not aware that the basis-substance ("intercellular substance") itself contains a large amount of living matter, and consequently held that the inflammatory corpuscles are an offspring of the "connective-tissue cell" and its coarser offshoots only. Neither did he know that at first

* "Studien über den Bau und das Leben der capill. Blutgefässe." Sitzungsber. d. Wiener Akad. d. Wissensch, 1865.

† "Ueber Entzündung und Eiterung." Virchow's Archiv, Bd. xl.

‡ "Studien aus dem Institute f. Experimentelle Pathologie in Wien," 1870. And a number of articles of Stricker and his pupils in "Wiener Mediz. Jahrbücher," 1871-1881.

most of the inflammatory corpuscles remain united by delicate spoke-like offshoots, giving rise eventually to a new formation of tissue, consequently he considered the inflammatory corpuscles and the pus-corpuscles to be one and the same thing, and inflammation and suppuration as identical processes.

In 1872,* when I took up the study of inflammation, in Stricker's laboratory in Vienna, I adhered to the cell theory, and my explanations of the phenomena of inflammation were in accordance with this theory. One year later, however, I announced new discoveries concerning the structure of "protoplasm" and the basis-substance, and also concerning the intimate nature of the inflammatory process.† The articles in this chapter on inflammation of the connective tissue are translations of my papers which were published in 1872 and 1873—the former being modified in accordance with the bioplasson views, the observed facts, however, and their description remaining unaltered. Instead of "protoplasm" I shall use the term "bioplasson." The inflammation of the myxomatous variety of connective tissue is not dwelt upon in the following articles. I refer to the article "Pulpitis," by Boedecker.

1. Inflammation of Connective Tissue.

(A) Inflammation of the Periosteum. On artificially producing inflammation in the bone of a mammal,—my experiments were made on dogs, cats, and rabbits,—inflammation in the periosteum, in the neighborhood of the injured part, was also induced, as a rule. The appearances are identical, whether the inflammation occurs in the calcified or in the non-calcified, the fibrous or the ribboned periosteum. A specimen furnished by the periosteum of the scapula of a grown cat, on the third day of inflammation, after having been preserved in a solution of chromic acid, represented the features seen in Fig. 149.

We notice that, instead of the fibrous and ribboned structure of the periosteum, a number of partly globular, partly fusiform, elements are present, which are mostly nucleated, and grouped in rhomboidal fields.

An analysis of the elements gives the following result: some of them contain a central lump of a bright yellowish color, either homogeneous or pierced by vacuoles, and around it a pale, finely granular zone. Other elements are found besides the homogeneous lump; these have but one pale nucleus, of varying size and globular shape. In a vesicular nucleus of this kind we notice sometimes one larger and sometimes several smaller nucleoli. Lastly,

* Studien am Knochen u Knorpel. Wiener Mediz. Jahrb., 1872. Ueber die Rück-u Neubildung von Blutgefässen im Knochen u. Knorpel. Wiener Mediz. Jahrb., 1873.

† "Untersuchungen über das Protoplasma. v. Die Entzündung der Beinhaut, des Knochens und des Knorpels." Sitzungsber. d. Wiener Akad. d. Wissensch., Juli. 1873.

we meet with elements in which we observe, instead of nuclei, formations, standing apart, which have characteristics of nucleoli. Between the rhomboidal groups of the above-described elements we see narrow, fusiform corpuscles, perhaps flat spindles, seen on edge. The interstices between the single elements of all varieties produce narrow, light rims, all of which are traversed by transverse, extremely delicate, grayish lines.

The periosteum here is evidently broken into elements, iden-

FIG. 149.—PERIOSTITIS OF THE SCAPULA OF A GROWN CAT, THIRD DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

N, nucleated plastid L^1, solid lump of the aspect of a nucleolus; L^2, plastid with partly homogeneous, partly reticular, formations, of the aspect of nucleoli, L^3, vacuoled bioplasson lump, surrounded by a bright rim of homogeneous bioplasson Magnified 800 diameters.

tical with those which lay the foundation for the development of the periosteal tissue.

All these features were still more prominent in specimens which I obtained on the fifth day of inflammation from the periosteum of a young, grown cat, after subcutaneous fracture of the leg bones. In the inflamed periosteum, the elastic strips which divide the tissue into rhomboidal ribbons could be recognized. Some of

these ribbons are composed of rows of globular elements; others are broken up into a number of fusiform corpuscles, and again others are in part made up of these corpuscles, while another part retains the character of a periosteal ribbon. The transition of granular corpuscles into periosteal rhombs, which are infiltrated with basis-substance, and look apparently homogeneous, is nowhere abrupt. The images of either variety may, to such

E—

FIG. 150.—PERIOSTITIS OF THE FRACTURED TIBIA OF A GROWN CAT. FIFTH DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

E, elastic stripe; *PP*, globular and nucleated plastids, sprung from ribbons of the periosteum *R*, transition of the basis-substance into free bioplasson. Magnified 800 diameters.

an extent, merge into one another, that even a single rhomb may appear in part pale and granular, and in part homogeneous, like basis-substance. In this specimen the single protoplasmic corpuscles, without exception, also exhibit the features described above. (See Fig. 150.)

At the point of the most intense inflammation, in the periosteum under consideration, extensive fields are transformed into

numerous globular elements, which are especially crowded in the vicinity of the blood-vessels. In the parts situated between the blood-vessels groups of elements or single corpuscles are found, surrounded by a zone of basis-substance, which in the chromic acid specimen has a homogeneous appearance, and bears a close resemblance to normal medullary tissue. Groups of inflammatory corpuscles give rise to a cartilaginous tissue. This fact can be ascertained by observation of the forming callus in the later days of the inflammation.

In the cartilaginous callus, which is the offspring of the inflamed periosteum, we sometimes see in a basis-substance, which is usually striated, large, pale, nucleated bioplasson bodies. Frequently we find smaller, yellowish, shining lumps, perforated with vacuoles, and sometimes lumps composed of such yellow granules. Finally, small cavities are observed in the basis-substance, which contain but one small bright-yellowish lump. (For illustrations, see article on "Healing Process of Fractured Bones.")

The structure of this callus-tissue is in every particular identical with that of normal cartilage. The only difference is that in the callus all corpuscles and their nuclei contain, at the points of intersection of the reticulum of living matter, very shining, yellowish granules, either single or in groups. These bodies evidently represent the juvenile condition of the bioplasson. The newly formed cartilage tissue is traversed by straight, glistening fibers, which divide the tissue into rhomboidal fields of varying size. These elastic fibers belonged originally to the periosteal tissue, and remained unaltered by the inflammatory process. They are recognized as such even in calcified portions of the cartilage; they, without any apparent regularity, traverse both the calcified basis-substance and the newly formed medullary spaces. That the process of inflammation in periosteum can produce not only medullary corpuscles and cartilage tissue, but red blood-corpuscles also, I propose to demonstrate in the next articles.

Since having made the above observations, I have seen exactly the same changes in the inflammation of fibrous connective tissue in the derma of the skin, the pericementum of the tooth, and in many other localities (see corresponding articles). The process was materially the same. First a dissolution of the basis-substance took place, which led to a freeing and reappearance of the bioplasson, previously concealed in the basis-substance. Next by an outgrowth of single granules of bioplasson new elements arose,

in an amount greatly exceeding the original number of plastids. At last, after the inflammation had subsided, a new infiltration with basis-substance ensued, and consequently a new formation of connective tissue took place — unless the inflamed tissue, from the condition of free bioplasson, immediately fell back into the basis-substance-forming stage. Similar features are observed in inflammation of the tendinous and peritendinous tissue of the horse, termed by veterinary surgeons "softening of tendons." (See Fig. 151.) The original dense fibrous connective tissue, containing only a small number of plastids, is gradually transformed into a more homogeneous basis-substance, in which numerous plastids of varying sizes have made their appearance. That these newly appearing plastids have not originated from former plastids of the connective tissue, but arose independently after liquefaction of the basis-substance at certain points, which at first were nearly regularly

FIG. 151.—PERITENDINITIS IN A HORSE.

B, fibrous basis-substance with a few plastids; *M*, the basis-substance more homogeneous, with numerous, newly appeared, nucleated plastids, *I*, the basis-substance transformed into rows of nucleated plastids, or multinuclear bioplasson masses; *A*, artery, cut transversely, containing a few blood-corpuscles. Magnified 800 diameters.

distributed throughout the basis-substance, is plainly demonstrated by all specimens of this kind. The whole basis-substance returns to its bioplasson condition — *i. e.*, is transformed into rows of plastids or into multinuclear bioplasson masses, before any new formation proper has taken place. It may be easily understood how this slowly advancing inflammation, not going beyond the stage of liquefaction of the basis-substance and the return to the bioplasson condition, might lead to a gradual "softening" of the tendon tissue.

(B) Inflammation of Cartilage. After irritation of cartilage tissue, the action which ensues depends upon the intensity and depth of the injury, as well as upon the locality to which the irritating agent was applied. In order to render the conditions uniform in all experiments, I chose the articular cartilage of the condyles of the femurs of chloroformed dogs, cats, and rabbits, which I injured with a red-hot pointed piece of iron.

Superficial Injuries in the Middle of the Condyle. Twenty-six hours after the injury, I found the excavation produced by the iron partly covered with an eschar, and the tissue in the neighborhood of a grayish yellow color. A few cartilage cavities were enlarged, and contained a finely granular, sometimes vacuoled, mass.

In specimens obtained on the fifth day of inflammation of the articular cartilage, I found, close to the border of the injured place, large cavities, in part open toward the surface, surpassing in size the normal cartilage cavities sometimes by five diameters. Between these enlarged cavities the basis-substance was reduced to narrow septa. The cavities contained a pale granular substance, divided into fields and nucleated corpuscles. I was unable to determine whether these had originated from a single enlarged corpuscle, or by simple reduction of the basis-substance between the original cartilage corpuscles. The latter view was supported by the fact that sometimes several corpuscles were seen occupying the larger cavities, surrounded by a narrowed basis-substance. Close to the changed zone, around the injury, unaltered cavities were observed, which held unchanged corpuscles.

The appearances were the same, after the inflammation had lasted for eight days, in specimens taken from the knee-joint of an old rabbit, in which, in consequence of the injury, suppuration had occurred. The spindle-shape of some of the cartilage corpuscles which lay close to the border of the wound could be accounted for by the mechanical pressure of the iron rod used in producing the inflammation. The result was such that in the middle of the articular cartilage, even by the most intense irritation, only slight changes could be produced in the cartilage tissue. These changes consisted in an enlargement of both the cartilage corpuscles and their cavities, while a formation of pus-corpuscles could not be obtained.

One year afterward, the late Prof. Rokitansky kindly placed in my hands the second right rib of a man about twenty-five years old, who, in a drunken brawl, had had the cartilage completely cut through six weeks before death.

The wound looked fresh, just as if produced but the day before; even the rust-spots from the knife were still visible. The perichondrium was thickened and held the two severed ends of the rib cartilage. Microscopic examination showed enlargement of some of the corpuscles close to the edge of the wound, but no other pathological changes.

Simultaneous Injuries of the Articular Cartilage and the Subjacent Epiphyseal Bone. Upon boring a hole into the cartilage, and penetrating the bone with the red-hot iron, a very striking phenomenon occurred—namely, a deposition of lime-salts in the cartilage, around the seat of injury. This feature, which was known to Redfern,* could be demonstrated after twenty-six hours, and recognized by the naked eye on the third day. The deposition of lime-salts was broadest at the border of the bone, and gradually became narrower toward the surface.

Close examination revealed the lime-salts deposited in the basis-substance of the cartilage, and in this situation most of the corpuscles had assumed an irregular, jagged appearance, due to offshoots arranged after the manner of a delicate net-work. At the boundary of the calcification, I met with cartilage cavities, surrounded either by unchanged basis-substance or by a calcified ring, which, as a rule, broadened toward the fields of general calcification, and was separated from these fields by coarsely granular depositions of lime-salts. (See Fig. 152.)

FIG. 152.—CALCIFIED CARTILAGE OF A MIDDLE-SIZED RABBIT, AFTER A SIMULTANEOUS INJURY OF THE ARTICULAR CARTILAGE AND THE BONE. [PUBLISHED IN 1873.]

P, bright, yellowish cartilage corpuscles, traversed by vacuoles; *B*, non-calcified basis-substance, with radiating offshoots of the cartilage corpuscles; *C*, calcified basis-substance at the boundaries of the territories. Magnified 800 diameters.

After decalcification of such specimens, it was apparent that the corpuscles next to the border of calcification had become, either in part or wholly, transformed into homogeneous or vacuoled, yellowish, shining lumps—viz.: had returned to a juvenile stage.

Beginning from the third day of inflammation in the calcified portion, spaces were found, which were larger and more numerous nearer the bone than in other localities. These medullary spaces invariably started from the portion adjacent to the bone-tissue. The basis-substance being liquefied, the newly appearing corpuscles

* "Anormal Nutrition in the Articular Cartilages," London, 1850.

had either assumed a spindle shape or were fused into nucleated bioplasson masses, with a simultaneous production of blood-corpuscles and blood-vessels in the middle of the medullary space. Close to the border of these spaces the corpuscles exhibited no other changes than those above described. The epiphyseal bone, by dissolution of its basis-substance and increase of the corpuscles, also appeared to be provided with medullary spaces, and the perforation made by the iron was, after several days' inflammation, filled with nucleated masses and fusiform elements.

These experiments prove that a simultaneous injury of the cartilage and the bone is followed by a calcification of the cartilage along the border of the wound, and afterward by a dissolution of the calcified basis-substance, commencing in the vicinity of the bone and advancing toward the articular surface. The freed bioplasson behaves in a manner similar to that of inflamed bone.

Injuries at the Lateral Portions of the Articular Cartilage. The nearer the lateral edge of the articular cartilage the hot iron was applied, the more intense were the changes in the endothelium, in the synovial membrane, in the fibrous cartilage, and in the neighboring periosteum and tendons.

At the edge of the condyle of a young cat, on the second day after the injury, the tissues covering the cartilage were thickened and rendered cloudy by a considerable infiltration with inflammatory corpuscles. The tissue of the synovial membrane and the periosteum exhibited groups of corpuscles, which in some places were so crowded that only slight remnants of the fibrous bundles were visible.

In specimens of a young rabbit, from the sixth day of inflammation, the surface of the cartilage was covered with a continuous, freely nucleated layer of bioplasson, which was not sharply marked from the subjacent cartilage tissue. The cavity of the wound of the cartilage was found to contain along its borders numerous tracts of corpuscles, closely packed together, and uniting with analogous tracts proceeding from the subjacent bone. (See Fig. 153.)

Upon examining hyaline cartilage at points where it passed into the fibrous variety, and into periosteum, I recognized large cavities filled with corpuscles, containing large nuclei, often so closely arranged that the boundaries between the corpuscles could not be distinguished. Similar formations were found also at the border of the scapula of a young dog, on the fifth day

after the injury, but only in that portion of the cartilage lying nearest the osseous border.

With an augmentation of the corpuscles, a retrogression of the bioplasson to the juvenile condition takes place. As red blood-corpuscles are formed out of this bioplasson substance, I have termed it "hæmatoblastic." This rejuvenescence and transformation into red blood-corpuscles occurs in the inflammatory process, not only in cartilage corpuscles, but also in the corpuscles of synovial membrane, periosteum, and tendon. (See Fig. 154.)

FIG. 153.—CONDYLE OF FEMUR OF AN OLD RABBIT, ON THE EIGHTH DA[Y] OF INFLAMMATION, PRODUCED BY INJURY AT THE LATERAL SURFAC[E]. [PUBLISHED IN 1873.]

EC, unchanged cartilage; *IN*, large medullary space in place of the formerly calcified car-tilage; *T*, unchanged trabecula of bone; *IB*, medullary space in the bone-tissue, penetrating the calcified cartilage *MS*, unchanged vascular canal. Magnified 200 diameters.

Feeding of Cartilage-corpuscles with Insoluble, Granular Substances. I have injured with the red-hot iron the middle portion of the articular cartilage of the condyle of the femur, and that of the tibia of a young, nearly grown dog, and killed the animal seven days afterward. Around the jagged border of the wound

in a zone about two millimeters wide, I could see with the naked eye an intense brown discoloration of the cartilage. A similar discoloration was present on the tibia, though much less marked.

In horizontal sections from the condyle of the femur I found the basis-substance of the cartilage calcified around the wound, and the calcified zone broadened from the surface toward the bone. The calcified basis-substance appeared to be divided into

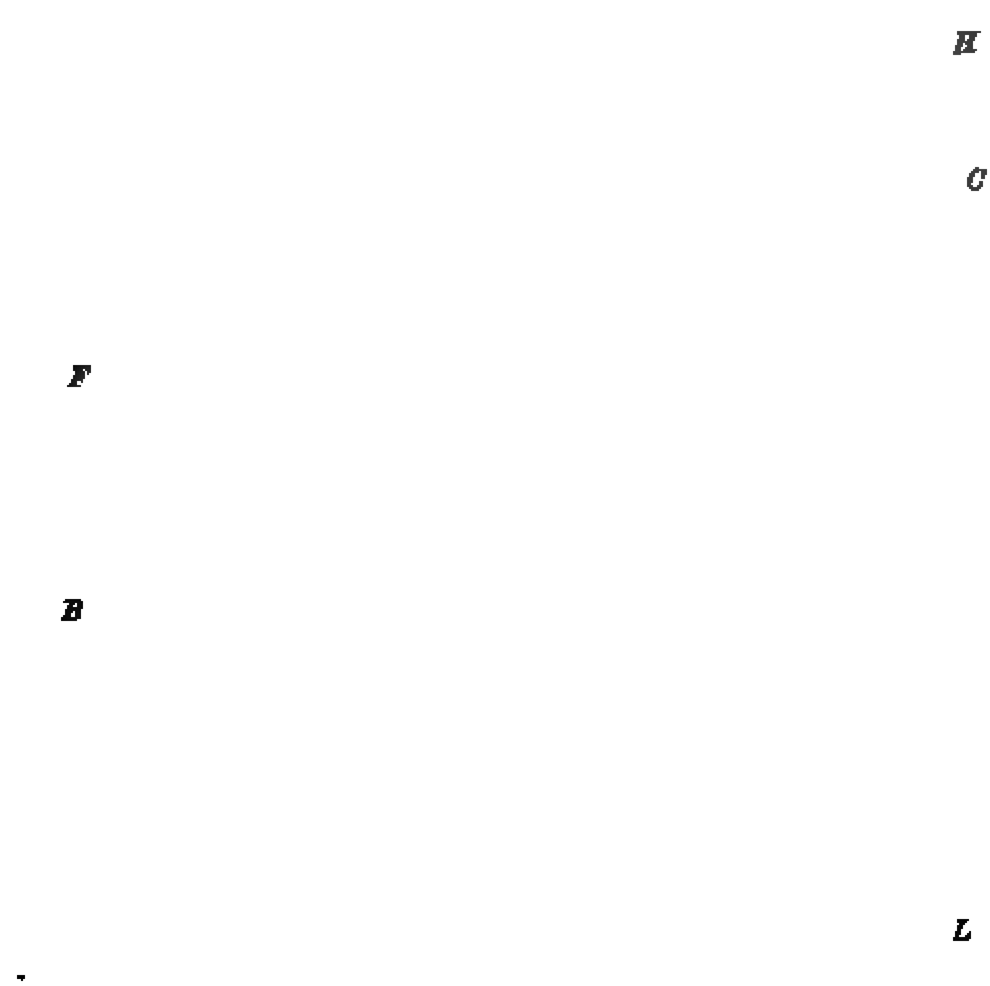


FIG. 154.—LATERAL SURFACE OF THE CONDYLE OF THE FEMUR OF A GROWN CAT, ON THE SEVENTH DAY OF INFLAMMATION. FRESH SPECIMEN. [PUBLISHED IN 1872.]

H, hyaline cartilage in transition to *F*, fibrous cartilage; *C*, greatly widened cavity, filled with inflammatory corpuscles, *B*, newly formed red blood-corpuscles, sprung from *L*, the bioplasson in a juvenile condition Magnified 800 diameters.

glistening, polyhedral fields of a brown color, which was more intense and wide-spread on the surface of the cartilage. Many of the cartilage corpuscles within the brown basis-substance

contained granules and lumps of a blackish-brown color, which were most numerous at a certain distance away from the border of the wound. Extremely minute black granules also were found in the basis-substance. That these granules were animal charcoal could éasily be determined by comparing them with the charred pastids attached to the surface of the wound, and with the eschar of the cartilage of other animals. But how did the charred granules penetrate the cartilage corpuscles? There must have been either a carbonification of certain parts of the corpuscle and the basis-substance, or else the coal particles had been transported from the surface of the wound toward the periphery.

The supposition of a partial carbonification was not sustained by experiments on other animals,—cats and rabbits,—and I never succeeded in producing brown granules in the corpuscles situated in the neighborhood of the burnt place of live or dead cartilage. *The conclusion, therefore, became admissible that the coal particles really were transmitted within the basis-substance by an active process of the cartilage corpuscles and their offshoots.*

Other experiments with powdered vegetable carbon and cinnabar, forced into fresh wounds of the cartilage, did not yield satisfactory results. I succeeded but once in demonstrating the presence of cinnabar granules in a cartilage corpuscle inclosed by an uninjured basis-substance. Cinnabar granules, on the contrary, which I had injected into the jugular vein, I invariably succeeded in finding in the cartilage corpuscles, within the district of inflammation, both in inflammatory corpuscles, filling the enlarged cartilage cavities, and also in cartilage corpuscles, apparently unchanged. I can, therefore, corroborate the assertions made by Reitz and Hutob.

In inflamed cartilage I have often seen red blood-corpuscles arising from both the corpuscles of cartilage and medulla. The insular and intravascular formation of red blood-corpuscles in some cases proved to be extremely active. After injuries inflicted on the lateral surface of the condyles, I observed enlarged fusiform cavities, which evidently had sprung from cartilage, partly or totally filled with initial forms of red blood-corpuscles—the "hæmotoblasts"—as well as with fully developed corpuscles. Solid bioplasson tracts sometimes directly connected the closed cavities of the above description, which were found in a large number, especially toward the tendon-tissue; they were sometimes hollow, and contained a single chain of red blood-corpuscles. The process of new formation of blood-vessels and blood proved to be identical with that noticed in inflamed bone-tissue, and for further particulars I refer to the article on inflammation of bone.

(C) *Inflammation of Bone.* Numerous experiments made during the years 1872 and 1873, on bones of dogs, cats, and rabbits, for the purpose of artificially producing inflammation, enabled me to obtain a general view of the phenomena of osteitis, from its incipient stage up to the eighth day. These are: first, the freeing of the bioplasson from its basis-substance; and, secondly, the return of the bioplasson to the juvenile condition.

In the earliest stages of the inflammation, twenty-six hours after the injury, also in the succeeding days, at the periphery of the inflamed district, a *dissolution of the lime-salts of the basis-substance takes place in bay-like fields;* this destructive process, however, does not invariably invade the whole of the territory, but often only part.

The decalcified basis-substance itself is next dissolved out, and in its place flat or globular bioplasson masses become visible, either single or coalesced into groups, exhibiting a number of nuclei, each of which corresponds to an original nucleus of a bone-corpuscle. Within these coalesced groups, new nuclei originate, and the multinuclear body presents the appearance formerly known under the name of a "myeloplax." (See Fig. 155.)

Such multinuclear bioplasson masses arise from one or several coalesced bone territories, and represent the bioplasson of the territory itself.*

A multinuclear body, at the periphery of the inflammatory district, may at once lay the foundation for the new formation of a bone territory; or it may, in the more central portions of the inflammatory district, divide into a number of corpuscles, each one of which is provided with a nucleus. The corpuscles, as well as the larger bioplasson layers, are separated from the neighboring kindred formations by light, narrow rims, which are traversed by transverse filaments. These filamentous formations are threads of living matter, by which all newly developed elements are connected with each other and also with neighboring bone-corpuscles not yet set free.

This series of changes may be observed in the middle of the bone-tissue, as well as at the borders of vascular canals. The dissolution of the decalcified basis-substance, as a rule, begins at

* The multinuclear bodies are by no means formations confined exclusively to the medullary tissue of bone. They may appear wherever territories (units) existed before the infiltration with basis-substance took place, or where the basis-substance, either in normal or in morbid processes, is slowly being dissolved out, and thus the units of the tissue made free.

the border of the lacuna, therefore in the circumference of the uninfiltrated bioplasson body,— the bone-corpuscle,— and advances outward toward the periphery of the territory. We can satisfy ourselves *that it is not the central bone-corpuscle itself alone which enlarges, but that, after a wasting or dissolution of the basis-substance has taken place, leading to the freeing of the bioplasson,*

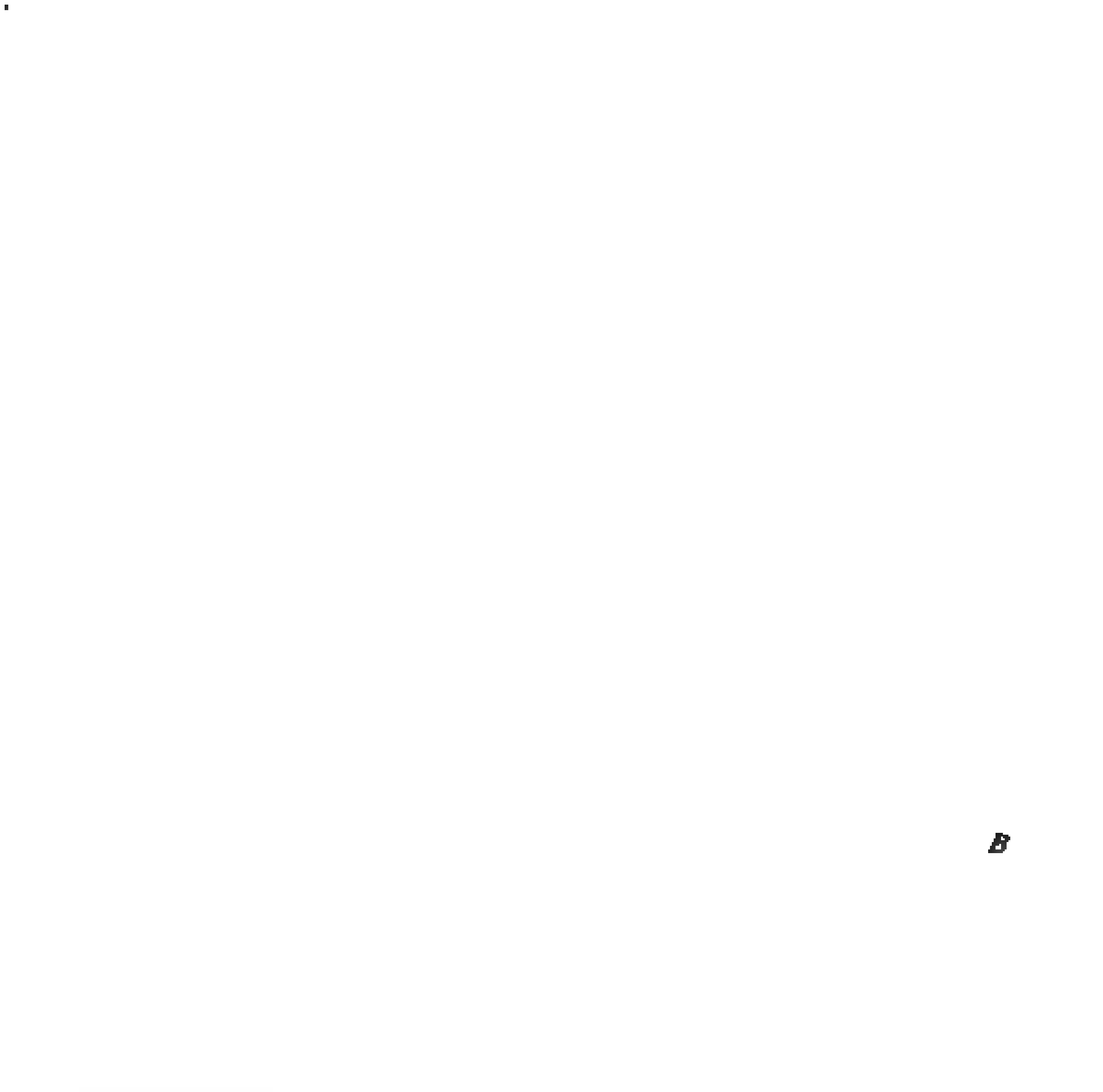


FIG. 155.—BAY-LIKE EXCAVATIONS, PRODUCED BY DISSOLUTION OF THE BASIS-SUBSTANCE, FROM THE TIBIA OF A DOG INJURED WITH RED-HOT IRON; EIGHTH DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1872.]

B, unchanged bone-tissue, with *C*, the bone-corpuscles; *P*, large nucleated bioplasson masses, filling the bays in connection with the unchanged bone, by means of delicate filaments. Magnified 800 diameters.

the latter, which before the inflammation was seen only in the bone-corpuscle, becomes visible throughout the whole territory. The next step in these phenomena is that the bioplasson contained in

the former osseous basis-substance now divides into a number of flat, fusiform, nucleated bodies. As a matter of course, it is the reticular bioplasson within the basis-substance, and not the basis-substance itself, furnishing the material for these elements, which are not really newly formed bodies, but only made visible and re-arranged in new groupings.

The final result of the melting or dissolution of the basis-substance is the appearance of medullary spaces. They may arise from bone-corpuscles and their surrounding basis-substance, independently of the vascular canals in the middle of the bone-tissue. This fact was known previously by Rokitansky. Medullary spaces may also have their origin in the borders of vascular canals, and the nearer the wound of the bone, the larger and the more irregularly excavated are the medullary spaces come from the vascular canals. They are always packed with globular or spindle-shaped corpuscles, while in their centers blood-vessels, containing blood-corpuscles, are found.

Running from the widened vascular canals, now transformed into medullary spaces, are channels filled with medullary corpuscles, which penetrate the interstices between the systems of lamellæ. The spaces which arise in the vicinity of the bone-corpuscles unite with those of the widened vascular canals and interstices; and in intense inflammation, up to the eighth day, the formerly compact bone is transformed into a cancellous structure—*i. e.*, only narrow trabeculæ of unchanged bone are left, between which are large spaces containing medullary corpuscles. In still more intense inflammation, especially that produced by boring into the compact bone with a pointed hot iron, the bone-tissue in the district of inflammation around the wound is to a great extent transformed into medullary tissue, holding newly formed blood-vessels, and in this tissue, only very small, irregular islands of the former compact bone are found. Obviously, the juvenile condition of the bone is reëstablished by this process, even in its coarser anatomical relations. (See Fig. 156.)

The elements which have newly appeared bear a close resemblance, so far as their shapes are concerned, to those present in normal vascular canals, between the wall of the blood-vessel and the wall of bone. They are nothing more than medullary elements in the stage of indifference — eventually osteoblasts.

In slight degrees of inflammation, the medullary elements, up to the eighth day, may, at the surface of the inflamed bone, again be transformed into the so-called "osteoid" tissue by infiltration

with lime-salts. In this way are originated new trabeculæ, with a high degree of luster, between which, in irregularly arranged cavities, in part nucleated bioplasson bodies are left. In these recalcified basis-substance we can trace the former medullary corpuscles, as their general configuration is unaltered. The reticular structure of this basis-substance is distinctly visible without any re-agent, owing to the high degree of refraction of the fields, infiltrated with lime-salts. (See Fig. 157.)

The second series of changes concerns the bioplasson itself: *it returns in a relatively short time from the phase of advanced*

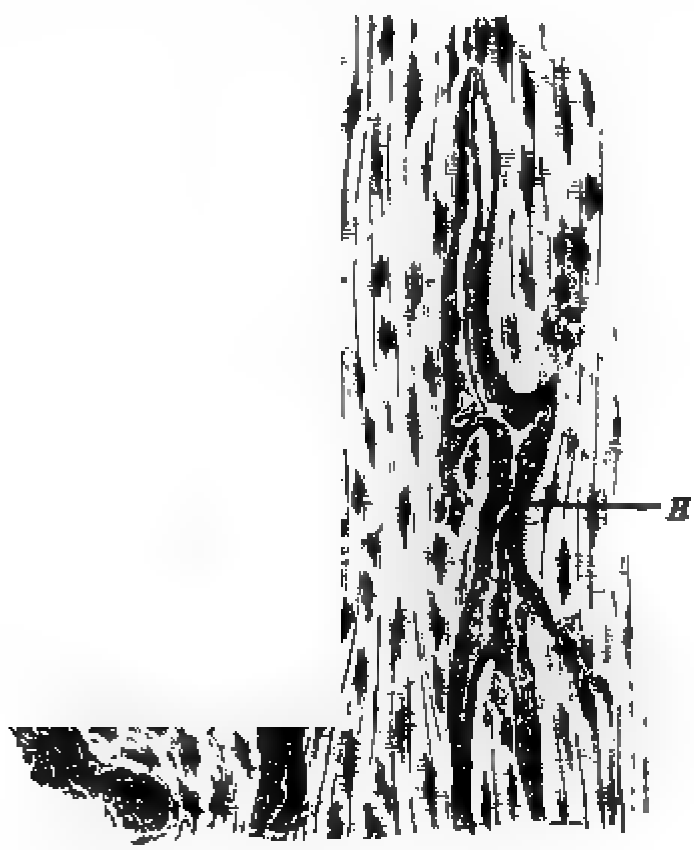


FIG. 156.—TRANSFORMATION OF COMPACT BONE INTO MEDULLARY TISSUE. TIBIA OF A DOG, EIGHTH DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN.

H, widened Haversian canal; *C*, projections of the compact bone, with considerably enlarged and apparently augmented bone-corpuscles; *I*, islands of bone; *M*, medullary tissue containing newly formed blood-vessels. Magnified 300 diameters.

development into the juvenile condition. This occurs before any other change, and is quite constantly observed in the homogeneous nucleus of plastids in the younger, and the nucleolus of those in older animals. The nucleus is transformed into a bright, yellowish body, which divides into several lumps. In the inflamed district, beginning from the second and third day of inflammation, we meet with bone-corpuscles, containing divided nuclei, even in unchanged osseous lamellæ.

Rejuvenescence may involve either the larger portion of bone-corpuscles or the whole corpuscle, and these bodies are partially or totally transformed into yellowish, shining lumps, which I formerly considered hæmatoblastic (see page 101). The dissolution of the basis-substance around the homogeneous lump takes place in the same manner, as described above.

The return to the juvenile condition, however, may at a comparatively early date invade not only the central bone-corpuscle, but also take place, to a greater or less extent, in the bioplasson, inclosed in the basis-substance. Some offshoots of the bone-corpuscle may become broader; in some of them even rejuvenescence may occur, independently of the central bioplasson body. Lastly, this change may affect the whole mass of bioplasson present in a territory, as illustrated by Fig. 40, page 126. Here the retrogressive change in the bioplasson preceded the dissolution of the basis-substance.

P

B

FIG. 157.—RECALCIFICATION OF THE MEDULLARY TISSUE OF A DOG'S TIBIA, INJURED WITH RED-HOT IRON, EIGHTH DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

P, large, nucleated bioplasson bodies. *B*, calcified basis-substance, exhibiting a distinct reticular structure. Magnified 800 diameters.

The result of the recurrence to the juvenile stage of development is different, according to its degree. A number of bright, homogeneous lumps may arise from the bioplasson of the bone-corpuscle, as well as from that of the basis-substance, and each lump, even the most minute, is enabled to produce a new element. This new formation, traceable step by step in the medullary spaces, is due to the differentiation of compact bioplasson into a reticulum, therefore an advance toward a higher stage. Each lump, or each element, under these circumstances, remains, by means of delicate filaments, in living connection with all its neighbors. (See Fig. 158.)

Should the division of young bioplasson into small lumps occur at a very early stage, and very rapidly, the formations which I have termed "hæmatoblasts" will be the result. Each hæmatoblast, by being severed from the neighboring elements,

and becoming dense at its periphery, may give rise to a colored blood-corpuscle. The newly formed blood-corpuscles either lie within and between other bioplasson bodies, or else they are inclosed by a shell of bioplasson which, by vacuolation, has

FIG. 158.—FRACTURED FIBULA OF A GROWN DOG, LONGITUDINAL SEC-TION. FOURTH DAY OF INFLAMMATION. CHROMIC ACID SPECI[MEN]. [PUBLISHED IN 1873.]

T, flat bioplasson bodies, in the stage of indifference, blending with the basis-substance bioplasson bodies (medullary corpuscles), sprung from both the bone-corpuscle and the b[asis-]substance. *S*, bioplasson bodies, with numerous bright lumps. *N*, original bone-corpu[scle] with enlarged nucleolus, and a partly solidified nucleus. Magnified 800 diameters.

become hollow. This represents the first trace of blood-vess[els] which, from their earliest stage, hold red blood-corpuscles.

The second series of changes in inflamed bone, describe[d]

above, lead to formations, constantly met with in the immediate vicinity of the inflammatory district. A number of newly formed medullary spaces are filled with yellowish, shining elements, which, in their form and the nature of the basis-substance surrounding them, are analogous to normal juvenile medullary corpuscles. In such spaces a more or less abundant new formation of red blood-corpuscles, and also, though not constantly, of blood-vessels, is going on; the spaces, as a rule, contain in their centers blood-corpuscles and blood-vessels, and at their periphery bioplasson bodies of varying size. Sometimes red blood-corpuscles originate in multinuclear bioplasson masses, as I described in 1872.

Finally, I emphasize that *the living connection of the bioplasson bodies, except the hæmatoblasts, is not interrupted in the non-purulent inflammation of bone. An isolation can be asserted to exist only in colored blood-corpuscles and in pus-corpuscles.* The blood-corpuscles float in a liquid whose origin is connected with a partial paling and waste of bioplasson. The formation of this liquid always occurs within the first vacuoles—*i. e.*, the first vascular tubes, and both the liquid and the newly formed red blood-corpuscles take part in the circulation as soon as the newly formed vessels join the older ones. It has been proved by Rustizky* that from the freed bioplasson in the process of inflammation of bone, pus-corpuscles also originate.

New Formation of Blood-vessels in Inflamed Bone-tissue.† In bone in which inflammation is artificially induced, a very active new formation of blood-vessels takes place.‡ These are mostly capillaries arising from the elements of the decalcified, but not dissolved, bone-tissue, and in medullary spaces originating from the derivations of the bone-tissue—viz., the medullary corpuscles.

* "Untersuchungen über Knocheneiterung." Wiener Mediz. Jahrbücher, 1871.

† "Ueber die Rück- u. Neubildung von Blutgefässen im Knochen u. Knorpel." Wiener Mediz. Jahrbücher, 1873.

‡ R. Volkmann (Langenbeck's Archiv f. Klinische Chirurgie, IV. Bd. 1863) describes a new formation of vascular canals in the compact substance of bone, occurring in so-called "vascular ostitis." What this author describes is not identical with what I have seen, for he maintains that in the formation of vascular canals the bone-corpuscles take only an accidental part, or do not participate in the least. How the vessels themselves are formed he does not say.

H. Lossen (Virchow's Archiv, Bd. lv., 1872) attempts to demonstrate, in specimens obtained from dry bone, that the canalization of bone-tissue really starts from bone-corpuscles.

At the surface of the injured scapula of a dog, on the fourth day of inflammation, I met with well-marked features indicative of a new formation of blood-corpuscles and blood-vessels. (See Fig. 159.)

I saw enlarged cavities in the basis-substance, deprived of lime-salts, containing a number of bright, yellowish, homogeneous lumps and disks, which might be properly termed "hæmatoblasts" (see page 100). Some of these lumps were vacuoled,

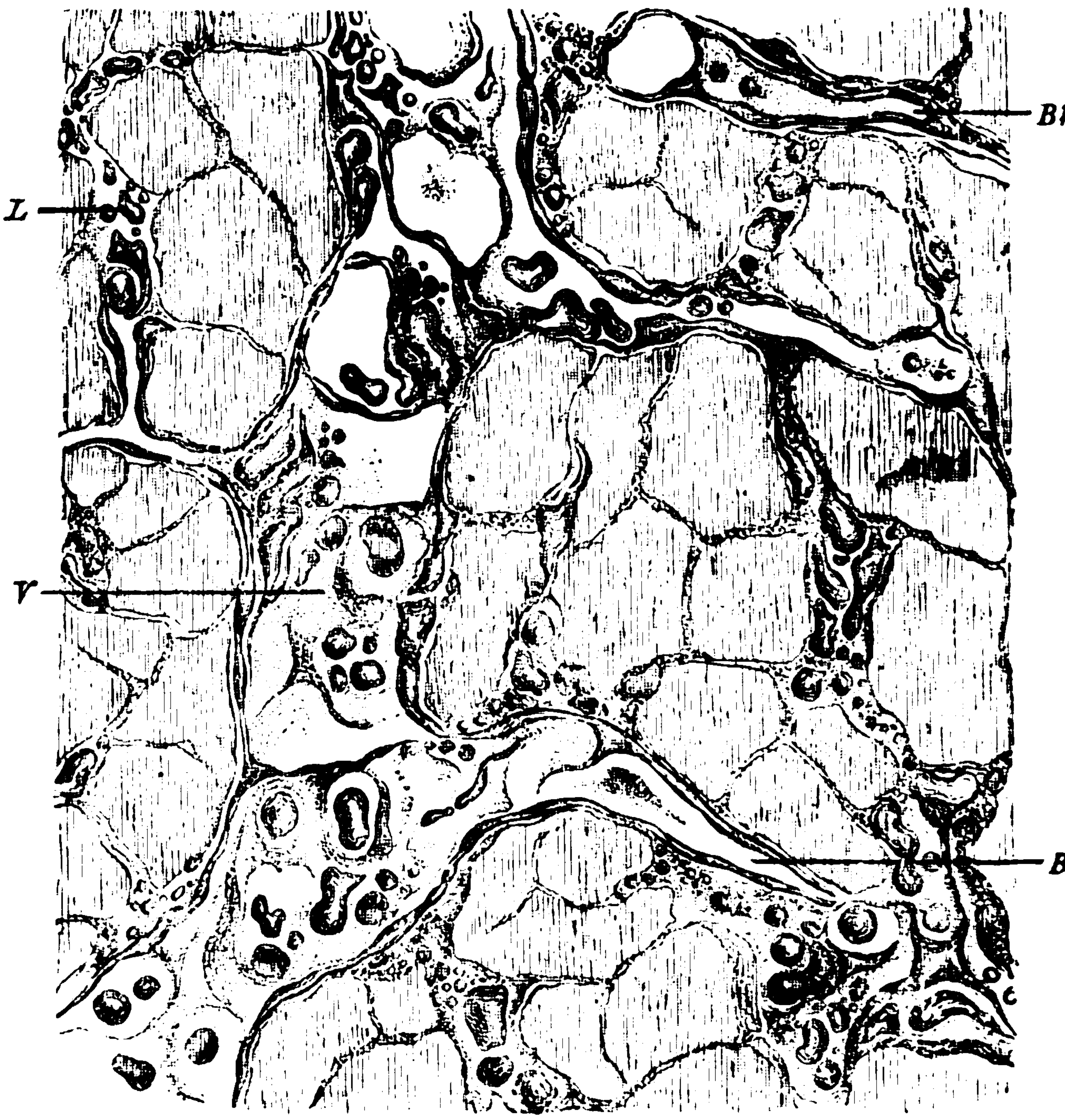


FIG. 159.—SCAPULA PLATE OF A DOG, ON THE FOURTH DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

L, lumps of bioplasson in a cavity partly inclosed by an investment of bioplasson; *V*, elongated and vacuoled bioplasson tube, traversed by septa and containing isolated lumps, the hæmatoblasts; B^1 and B^2, offshoots of the bioplasson tube, terminating blindly. Magnified 800 diameters.

others vacuoled and elongated, and, again, others considerably enlarged by vacuolation. In all cavities produced by vacuolation, isolated hæmatoblasts in varying numbers could be seen beside a pale granular mass. By coalescence of vacuoled bioplasson bodies tubular formations originated, which were divided into

number of chambers by transverse or oblique septa, the remnants of the hollowed bodies. The septa eventually disappearing by liquefaction and wasting of the bioplasson, a common caliber is established, irregularly bounded by flattened layers of unchanged bioplasson, exhibiting in their optical diameter a number of nodulations. This tube is in a direct communication with hollow offshoots, exhibiting the same features, and terminating either blindly or in cavities destitute of a bounding layer, but containing hæmatoblasts.

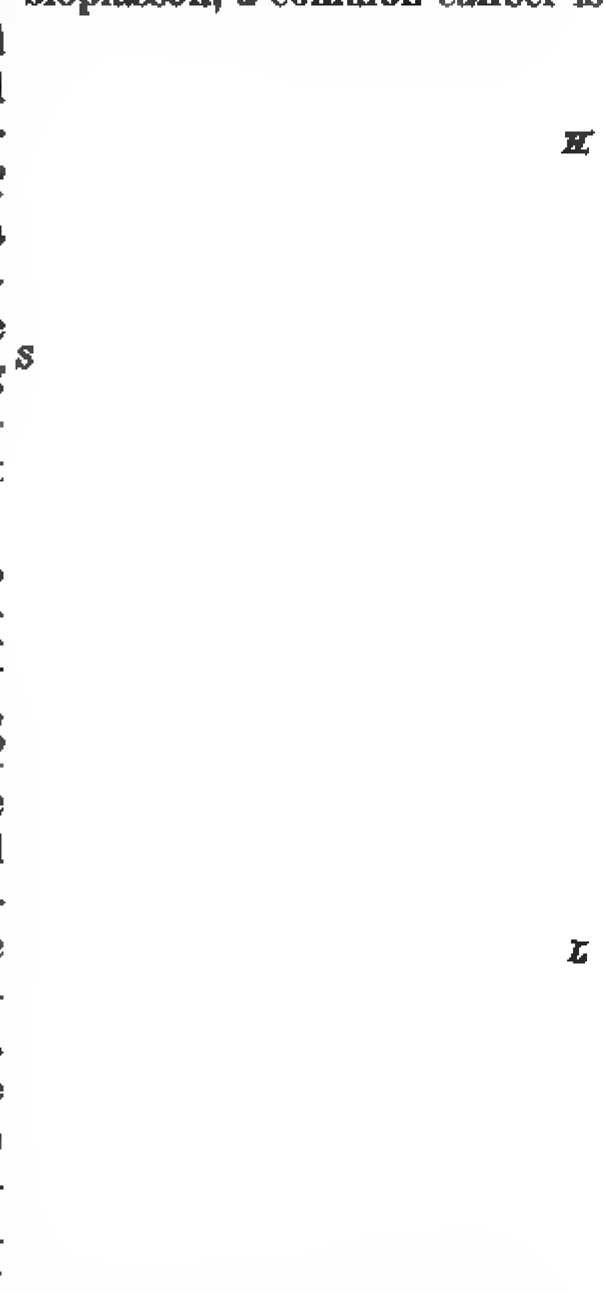


FIG. 160.—SCAPULA PLATE OF A CAT, ON THE THIRD DAY OF INFLAMMATION. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

Newly forming blood-vessel, terminating in a vacuoled plastid, *L*; *S*, remnant of a former septum; *H*, lumps of bioplasson—the hæmatoblasts entangled in finely granular, coagulated albumen. Magnified 800 diameters.

In the scapula plate of a cat, on the third day of the artificially induced inflammation, I observed solid bioplasson tracts, which arose from the border of a medullary space, ran along the lamellæ, and connected several enlarged and homogeneous bone-corpuscles. Not infrequently the bone-corpuscle next to the medullary space was most enlarged, and appeared hollow, while the distant corpuscles of the chain were solid. I also observed finished tubules, terminating in a solid point and traversed by transverse septa or their remnants, indicative of the origin of the tubule. Such tubules always contained a varying number of isolated solid bioplasson lumps,—the "hæmatoblasts,"—together with finely granular, coagulated albumen. (See Fig. 160.)

In many specimens obtained from inflamed bone, up to the fifth day of inflammation, I observed similar formations in the newly formed medullary spaces also. In all cases, first, solid

bioplasson tracts were seen, which, by vacuolation, became hollowed, often exhibiting transverse septa,—the remnants of the walls of the vacuoles,—and containing hæmatoblasts. From the walls of these forming blood-vessels, solid buds or fusiform or club-shaped prolongations arose, which indicated the formation of new, collateral branches of blood-vessels. Not all the red blood-corpuscles found in medullary spaces were inclosed in blood-vessels, for I often met with blood-corpuscles, isolated or in groups, among the medullary elements which had sprung from inflamed bone-tissue, without a trace of an investing bioplasson layer. Such corpuscles evidently are never carried into the circulation, and I was unable to discover either their office or destiny.

Often, multinuclear bioplasson masses were found, holding in their substance a varying number of red blood-corpuscles. Several times I observed an outer investment of spindle-shaped bodies, which surrounded the multinuclear masses. Sometimes the spindle-shaped bodies produced a well-marked, broad layer around these masses, which had been partly changed into a homogeneous or finely granular, possibly liquid, substance. Along the investing layer, inside the caliber, wreaths of hæmatoblasts were seen. All these features indicated the formation of veins; but I was not able to determine that the investing spindles were muscle formations.

That in inflamed tissues a new formation of arteries occurs I am certain from a specimen of Prof. Stricker's, who, in 1871, showed me an inflamed cornea—I cannot recall whether of a frog or a rabbit—in which a newly formed artery could be positively diagnosticated.

Conclusions arrived at in 1873. Inflammation was considered by humoral pathologists to consist essentially in a diseased condition of the blood and an exudation of its plasma; while cellular pathologists located the disease predominantly in the "individuals," the "tissue-cells." The latter view, announced by Virchow, was the leading one up to our time.

The presence of an *exudation*, the altered liquid of the blood, in the inflammatory process, needs to-day no special proof. It has never been doubted. The phenomena in the inflammation of bone could not be explained without the presence of a liquid which causes a dissolution first of the lime-salts and afterward of the glue-yielding basis-substance. Inflamed cartilage tissue likewise furnishes important proofs of the presence of an exudation. The fact that injuries entirely confined to hyaline cartilage pro-

duce trifling changes, while, if cartilage and bone be injured simultaneously, very marked changes occur at once in the cartilage tissue, indicates a direct dependence of inflammatory changes on blood-vessels. The rapid deposition of lime-salts in the latter case can scarcely take place from any other source than from a liquid introduced into the cartilage corpuscles. Upon boring into the cartilage and the bone, lime-salts are deposited in the basis-substance of the cartilage, at the border of the perforation, in a zone which broadens as it approaches the bone. This proves that the aperture is inundated with a liquid, flowing from the blood-vessels of the injured bone, from which the living matter of the cartilage derives the lime, originally kept in solution, ultimately to be deposited in the chondrogenous basis-substance.

Neither the sum of facts so far known to occur in inflammation of cartilage, nor the observations in keratitis, furnish any foundation for overthrowing the theory of exudation, and of the participation of the blood and the blood-vessels in the inflammatory process.

As regards the changes of the assumed "individuals," the "cells," this is a different matter.

Stricker was the first who positively declared that the cells by inflammation are reduced to a juvenile condition, in which they are enabled to proliferate. This assertion was based upon the observation of the changes which take place in the "protoplasmic body"—namely, its swelling, its becoming amœboid, the formation of new nuclei and new corpuscles from the older ones, and also the wasting of the "intercellular substance."

This view, with all that it involves, can be maintained, not only so far as the cells are concerned, but also for the inflamed tissue in general. *Every tissue, by the inflammatory process, is reduced to the condition in which it existed in the first stage of its development—that is to say, to a condition corresponding to its embryonal state.*

Thus bone-tissue, in inflammation, is dissolved into the elements from which it originated. Through the dissolution of the basis-substance medullary spaces are formed in the bone, at certain distances, which give to the inflamed bone of an animal, no matter how old, the appearances found in a newly born individual. In addition to this, in inflammation the basis-substance loses its lamellated structure, and in part assumes a striated aspect, which again corresponds to the bone of a new-born

animal. Finally, the medullary spaces are filled with elements identical to those from which bone-tissue originated.

The same is the case with periosteum and cartilage. The periosteal ribbons, whose boundaries remain marked by unchanged "elastic fibers," are dissolved and form rows and groups of globular and fusiform corpuscles, which correspond with the original formers of periosteum, not only as regards their shape, but in every particular. By inflammation cartilage is transformed into medullary elements, such as originally composed its tissue.

The totality of the elements observed in the inflammatory process has been designated by the terms "inflammatory new formation," "granulation tissue," and "suppuration." Recently, every newly appearing element was termed simply a "pus-corpuscle."

My own observations prove that the *newly appearing* elements at first are nothing but the elements of the tissue themselves. The term "inflammatory new formation" is applicable only in the later stages of the inflammation, when really *newly produced* corpuscles have originated from the freed mass of living matter.

The designation "granulation tissue" is scarcely tenable for the earliest stages of the inflammation, inasmuch as there is no new tissue produced, but only a formation analogous to that from which the inflamed tissue sprang—that is, a medullary tissue-formation for periosteum, cartilage, and bone.

The general designation of "inflammatory new formation," applied to "suppuration" or "formation of pus-corpuscles," is decidedly incorrect. The results of my researches show that the newly appearing, as well as the newly formed, elements are connected uninterruptedly by filaments of living matter, both with each other and with the non-inflamed neighboring tissue.

If in inflammation of a tissue single corpuscles become separated from their neighbors, and the so-called "migrating cells" are produced, their locomotion is evidently only a transient action. The newly formed red blood-corpuscles lying within their newly formed vessels, and which in a later stage join the older vessels, are really separated from the parent soil.

Pus-corpuscles, on the contrary, are unquestionably isolated elements which are separated from each other by a liquid. Pus, however, is no tissue, and from it, so far as we know and it is generally admitted, new tissue will never arise.

There is a marked difference, therefore, between those processes which pathologists have termed "*plastic inflammation*," on

the one hand, and "*suppurative inflammation*" on the other; although it may be granted that these processes depend only on different degrees of irritation.

Let us consider the inflammatory changes of the *living matter* of the tissue-units. In inflammation, this matter is probably at first provided with a surplus of liquid nourishing material. The question whether this material is conveyed in spaces between the living matter and the basis-substance, or whether the liquid immediately enters the living matter,—*i. e.*, is imbibed by it—cannot be answered by direct observation. This fact, nevertheless, is certain, that the surplus nourishing liquid shows its effects generally in the youngest portion of the tissue-unit—viz.: in the *nucleolus* and the *nucleus* of the non-infiltrated corpuscle. This portion is usually the first to return to the juvenile condition; it is divided into a number of particles, as has been stated by Virchow.

The living matter inclosed in the basis substance, upon receiving the increased nourishing material, responds, as a rule, by a dissolution of its basis-substance. Next follows the reëstablishment of the juvenile condition in a certain number of centers, each of which represents a nucleus or a nucleolus; and thus the embryonal or juvenile stage of the tissue, as described above, is re-assumed. Nearer the inflammatory focus the recurrence of youth is established in a larger amount of living matter, which is transformed into compact masses. Each mass may divide, and each fraction may give rise to a new corpuscle. If the connection between these corpuscles remains intact, medullary tissue is the result; if, on the contrary, the connection is broken, the compact particles of living matter are *hæmatoblasts*, and, eventually, red blood-corpuscles.

The *formation of new elements* from larger masses of living matter, as can be directly proved, is accomplished in such a way that within these masses, at certain intervals, new boundaries arise, the so-called "marks of division," which depend upon the location of the compact centers. These boundaries are newly formed cement- or basis-substance, in which there are no reticular formations, but merely delicate spokes of living matter. Every newly formed inflammatory corpuscle corresponds to a central body, whose living matter retains its embryonal condition—viz.: to a nucleus or to several nucleoli.

Lastly, if in many places the connection of living matter be broken,—*i. e.*, the spokes uniting the single lumps be torn,—the

lumps become unfit for producing new elements, and are suspended in a liquid, viz.: serum, derived from the blood which constitutes suppuration proper. Pus, as is known, is destined to perish.

The facts above enumerated lead to the conclusion that a *cellular* pathology, according to the theory of Virchow, cannot be maintained, for in the tissues of the animal body there are no "individuals," no "cells," and consequently can be no isolated "cellular foci of disease."

Tissues are composed of living matter and its derivations. In the center of the tissue-unit the living matter remains unchanged, while at the periphery the living matter is infiltrated with basis-substance. The continuity of living matter is nowhere interrupted; the detrimental influence, therefore, which acts upon the central body will also directly or indirectly reach the whole tissue-unit, and *vice versa.**

The changes which occur in the inflammatory process consist, first, in a dissolution or liquefaction of the basis-substance, and, secondly, in an increased production of the living matter of its own kind. As I have previously demonstrated (see page 46), each lump of living matter, no matter how minute, is capable of producing its kind, consequently to grow and form a new element. This is true of isolated particles as well as of masses of living matter combined into tissues and organs.

It yet remains to be proved whether or not certain "free" exudations of the animal body contain a number of extremely minute, isolated lumps, which have been torn from connection with the diseased tissues, and whether or not such lumps, under certain conditions, are still viable and endowed in any degree with the capacity for reproduction. Together with the emigration of colorless blood-corpuscles, such lumps may, perhaps, be a source of the enormous new formation of pus-corpuscles.

It is always only the living matter within a tissue which is subject to disturbances of nutrition, whether it is surrounded by an interstitial liquid or by an interstitial solid basis-substance. The non-living basis substance may undergo different changes,

* Later researches have proved that the changes may take place under certain conditions, first in the tissue-unit, before any change in the plastid has yet occurred. Even a portion of the plastid may exhibit inflammatory changes, while the remaining portion continues in a nearly unchanged condition. (See article "Caries of Teeth, especially of Cementum.")

but it is living matter exclusively which is enabled to reproduce its kind, and therefore capable of producing the extensive new formations which give rise to new tissues, such as pseudo-membranes, callosities, vegetations, etc.

It is not the cell and not the living portion of the cell which alone grows and proliferates; in the tissue, everything that is endowed with life can do so, consequently that portion of living matter which is inclosed by basis-substance also grows and proliferates. To this extent, made clear by observations and inferences, as far as connective tissue is concerned, we return to the stand-point of Rokitansky, inasmuch as we admit that the so-called "intercellular substances" are endowed with the capacity of growth.

There is no reason, however, to speak hereafter of a humoral or solidar pathology, any more than of a cellular pathology. There exists but one pathology, and that is the pathology of living matter. That only which is alive can become the subject of disease.

THE HEALING PROCESS OF FRACTURED BONES.

In several of my publications, issued in 1873, and quoted in the foregoing articles, incidental references are made to the phenomena of the healing process in fractured bones, which I propose here to include in one article. Later writers on this subject* have advanced no new views, as they have not considered the inflammatory process in the light of the bioplasson theory.

My researches were made in the leg-bones of dogs, cats, and rabbits, which I fractured designedly while the animals were kept under anæsthesia. In all instances I produced a displacement of the broken ends, in order to induce a somewhat higher degree of inflammation—the covering skin always remaining intact. How the healing process of fractured bones progresses by primary intention—*i. e.*, when the broken ends are in close contact,—is not known. All the numerous observations and conclusions concerning healing by primary intention in the soft tissues require revision, as a thorough understanding of this process is possible only through a knowledge of the minute structure of the tissues involved. None of the authors have had

* J. Hofmokl, "Ueber Callusbildung." Wiener Mediz. Jahrbücher, 1874. Here an exhaustive account of the literature on this subject is found.

this knowledge, strange as it may appear. Through the kindness of Dr. J. Lewis Smith, of New York City, I obtained two fractured arm-bones of children, one of fourteen days', the other of about four weeks', standing. I learned from these specimens that the process of healing is in human bones identical with that observed in animals.

Upon fracturing the bones of an animal, hemorrhage is produced, on account of the rupture of blood-vessels in surrounding tissues, as well as those of the bone; the initial swelling of the tissues around the place of injury is known to surgeons to be due to the extravasation of blood. The subsequent fate of the extravated blood-corpuscles we do not know; what we call "absorption" of the blood is merely an expression of ignorance.

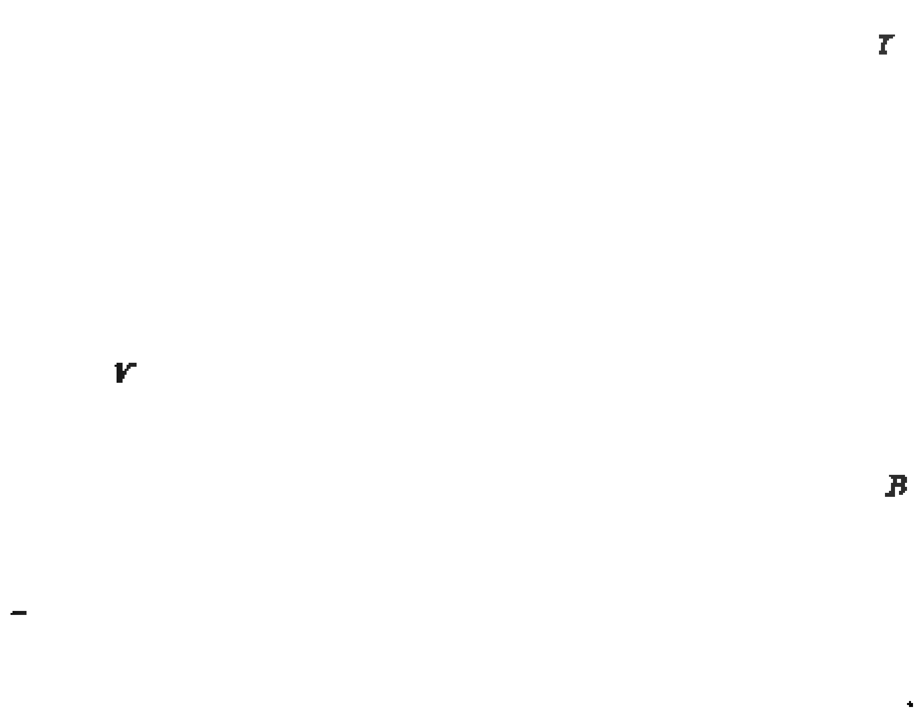
In the first few days following the injury inflammation sets in, varying in intensity with the degree of displacement of the ends of the fractured bone, and the general constitution of the animal operated upon. The inflammatory process is most active in the tissues which have the most abundant vascular supply—*i. e.*, the outer layer of the periosteum and the ruptured muscles, while it is less marked in the central medullary tissue of the bone, and still less in its compact portions.

The result of the inflammation, as described in former articles, is that the involved tissues, and mainly the periosteum, break down into medullary corpuscles, the same formation which originally contributed to produce the periosteal tissue. By an outgrowth of living matter, new medullary or inflammatory elements are afterward produced, all of which remaining in uninterrupted connection represent the *inflammatory new formation*. The compact bone-tissue, in the immediate vicinity of the fracture, is also melted out, and on the eighth day we see medullary spaces, which are more or less numerous, and filled with medullary or inflammatory corpuscles. These corpuscles are connected with the inflammatory tissue arising from the periosteum and the central marrow.

In the second week the inflammatory elements, being identical with medullary or embryonal corpuscles, form a new tissue, in a manner already dwelt upon in the chapter on formation of connective tissue. The result of tissue formation in this case is again identical with that observed in the earliest stages of embryonal life—*i. e.*, *the medullary tissue is transformed into cartilage*. Cartilage tissue appears after fractures, both of the human and animal bones, and constitutes the *provisional callus of*

Dupuytren. Whether such a provisional or cartilaginous callus is ever formed, when the broken bone-ends are closely fitting and the periosteum but slightly injured, has not been determined. This much is certain, however, that when a deviation of the bone-ends has occurred, the formation of provisional callus is invariably present.

The manner in which the inflammatory corpuscles are transformed into cartilage (see page 212) is briefly as follows:



G. 161.—CARTILAGINOUS CALLUS OF THE BROKEN TIBIA OF AN OLD CAT, FOURTEENTH DAY AFTER FRACTURE. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

B, slightly striated basis-substance, I, plastids in the stage of indifference, shortly fore the formation of basis-substance, V, capillary blood-vessel in the middle of a medul-y space. Magnified 800 diameters.

At the places most distant from the blood-vessels, the greater art of which are newly formed, the originally globular coruscles become elongated, and the nuclei of many of them disappear. This is caused by the splitting of the solid bioplasson of the nuclei into a reticulum, and the passing into the uniformly

"granular" stage of indifference. Usually such a change occurs without a preceding coalescence of corpuscles into territories. Many of the indifferent corpuscles become infiltrated with basis-substance; but we do not know whether this is of a gelatinous or chondrogenous character. Some, however, remain free from infiltration, at least in their central portions, and in this condition constitute the cartilage corpuscles which are found lying at nearly regular intervals throughout the newly formed basis-substance. In the second week after the injury, we invariably encounter nests of inflammatory corpuscles lying around a central blood-vessel. The corpuscles nearest the vessel are more globular, while the more distant ones are elongated and fusiform; we are able to trace all the stages of transition, from a uniformly reticular bioplasson into an apparently structureless basis-substance. (See Fig. 161.)

In the above-mentioned groups or nests of inflammatory elements we observe the transformation of capillary blood-vessels into solid cords, and subsequently the division of these into smaller medullary corpuscles, which in turn also share in the production of cartilage. This process is similar to the transmutation in advancing age of capillaries into tissue.

The newly formed basis-substance of the provisional callus is in part hyaline and in part striated. The striations are produced either by the preservation of the boundary lines of the former fusiform, indifferent elements, or by a splitting of these elements into small spindles, within the territory, before the infiltration with basis-substance had taken place. We notice bioplasson bodies at regular intervals, which in this stage deserve the name of cartilage corpuscles; they vary greatly both in size and appearance. In some cavities of the basis-substance we encounter large, pale, nucleated plastids; in others, smaller, shining lumps, usually with vacuoles; and in other cavities plastids are found which are composed of a varying number of lumps of different size. Lastly, very small cavities are seen in the basis-substance, containing only a single yellowish, bright lump. All plastids, whatever may be their size and shape, exhibit a distinct reticular bioplasson structure, whenever they are nucleated; all granules and lumps contained in a plastid are likewise interconnected, and from all plastids, without exception, delicate radiating spokes arise, which penetrate the surrounding narrow rim, and are lost in the basis-substance. (See Fig. 162.)

The newly formed cartilage of the provisional callus corre-

sponds in its structure with normal hyaline or striated cartilage. A striking difference, however, is displayed in the tissue of the provisional callus by the large amount of bioplasson it contains. The coarse granulation of even the nucleated plastids; the masses of bioplasson lumps lying in the cavities; the presence of single compact and vacuoled lumps in many of the cavities are all unquestionably due to the great augmentation of living matter produced by the inflammatory process. Such irregular formations are never met with in normal hyaline or striated cartilage. They can be explained only by the different phases of development which the bioplasson lumps undergo. (See page 46.)

That the newly formed cartilage has really to a great extent sprung from former periosteal tissue is proved by the presence of unchanged elastic fibers. The cartilage tissue is traversed by a varying number of single, sometimes bifurcating, straight, glistening fibers, which either divide the tissue into more or less regular rhomboidal fields, or are scattered through it without uniformity. There is scarcely any doubt that these elastic fibers originally belonged to the periosteal tissue, and remained unaltered by the inflammatory process. They also continue unchanged even after calcification of the cartilaginous tissue has taken place—nay, even after this tissue has retrogressed to the medullary state, the fibers often traversing the newly formed medullary spaces without any apparent regularity.

FIG. 162.—CARTILAGINOUS CALLUS, FOURTEEN DAYS AFTER THE SUBCUTANEOUS FRACTURE OF THE TIBIA OF AN OLD CAT. CHROMIC ACID SPECIMEN. [PUBLISHED IN 1873.]

a, plastid with several formations like nuclei, *b*, vacuoled, shining plastid, *c*, plastid, composed of numerous small, bright granules and lumps, *d*, minute bioplasson lump in a cavity of basis-substance. Magnified 800 diameters.

In the third week after the fracture, a calcareous deposition takes place in the tissue of the provisional callus. Its extent varies greatly in different individuals, and sometimes it is very scanty, though never entirely wanting. In the fractured humerus of a child, during the fourth week after the injury, the calcifica-

tion had pervaded a large amount of the newly formed cartilage, while in other places the formation of medullary spaces and of trabeculæ of bone was observed—the latter, however, only on a small scale.

Simultaneously with the deposition of lime-salts, and often independently of it, a peculiar change is observed, at nearly regular intervals, in certain points of the cartilage tissue—viz.: *the formation of red blood-corpuscles, of blood-vessels, and also of medullary tissue.* Those portions of the cartilage tissue which exhibit, in the basis-substance, at an earlier stage, the greatest number of small bioplasson lumps, and which have, to all appearance, sprung from former capillary blood-vessels, show the most marked new formations of blood and blood-vessels.

Nests of medullary or indifferent corpuscles, or multinuclear bioplasson masses, are found, exhibiting an active outgrowth of living matter. This divides into small lumps, which subsequently imbibe hæmoglobin, and constitute, first, hæmatoblasts and, later, red blood-corpuscles (see page 98). The peripheral portions of the plastids, or the multinuclear masses, are changed into flat, thickened layers of bioplasson, which lay the foundation of the walls of blood-vessels. Such a wall, in the optical section, exhibits slight fusiform thickenings, indicating, perhaps, the future nuclei of the endothelia. Club- and rosette-shaped formations of this kind are at first connected with older blood-vessels by means of solid, bright cords of living matter, which, after they are hollowed out, establish a communication between the newly formed blood-vessels and the older ones. (See Fig. 163.)

Together with the appearance of blood-corpuscles and blood-vessels, and the deposition of lime-salts in the basis-substance of the cartilage ("osteoid tissue" of authors), the new formation of medullary spaces is inaugurated. Around the newly formed blood-vessels, or independently of them, the cartilage tissue breaks down into medullary elements, solely in consequence of a dissolution or liquefaction of the basis-substance. The newly appearing medullary corpuscles are the same which, at an earlier date in the healing process of the fracture, produced the cartilage tissue.

By a continuous dissolution of the calcified basis-substance, the medullary spaces are enlarged and the medullary corpuscles augmented by a growth of living matter. In the central portions of the medullary space the corpuscles produce new blood-vessels, if such had not previously formed. The

ss is exactly like that of the normal dissolution of carti- which leads to the new formation of medullary tissue, and quently of bone.

eanwhile, at the fractured surfaces of the bone, similar llary spaces have formed in consequence of the dissolution e basis-substance of the bone and an increase of its bioplas- ıaterial. The connection of the irregular, bay-like medul- spaces of the bone with those of the adjacent calcified age can be traced directly.

·om the medullary tissue, which is the offspring of the

33.—Cartilaginous Callus, Eighteen Days after the Subcu- neous Fracture of the Tibia of a Cat. Chromic Acid Specimen. ublished in 1873.]

rtilage corpuscles in a striated basis-substance; *M*, elongated medullary plastids, toward the formation of basis-substance, or resulting from a dissolution of basis-sub- *B*¹, *B*², club-like spaces, lined by a continuous bioplasson layer, containing hæmato- ed red blood-corpuscles. Magnified 800 diameters.

ned periosteum, bone-tissue arises, in exactly the same man- s in the normal development of bone (see page 247). *This issue establishes the formation termed definitive callus (Du- en).*

ıe trabeculæ of bone in children and animals begin to r in the fourth week after the fracture; these at first are

very irregular formations, exhibiting an indistinctly striated, calcified basis-substance and very large and irregular bone-corpuscles. The medullary spaces are filled with medullary corpuscles, and contain, in their centers, newly formed blood-vessels, which are smaller the nearer they approach the compact structure of

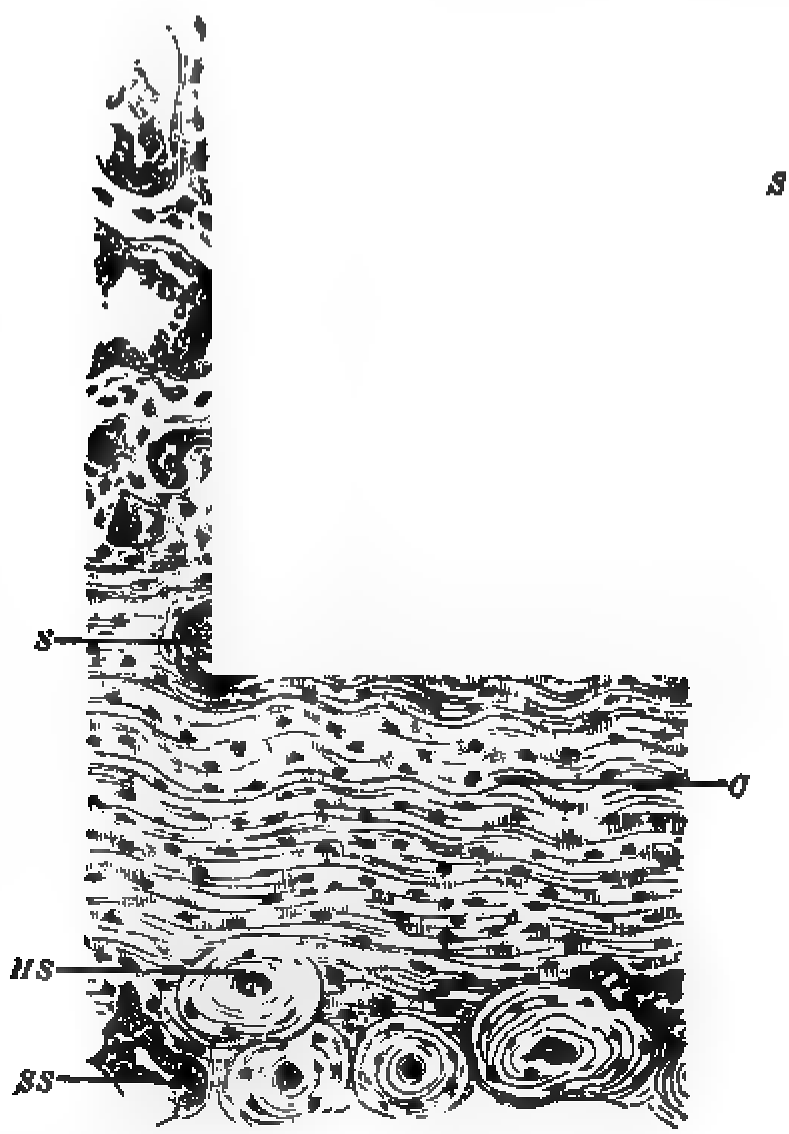


Fig. 164.—Exostosis after Periostitis of the Tibia of a Dog in Fifth Week of Inflammation; Identical in Structure with Definitive Callus. Chromic Acid Specimen.

C, superficial compact layer, with *HS*, the Haversian systems, and *SS*, newly formed medullary spaces; *H*, vascular canals, widened into medullary spaces, *S*; *T*, trabeculæ of newly formed bone, with large and irregular bone-corpuscles, inclosing large medullary spaces, *MS*. Magnified 200 diameters.

the injured bone. Unquestionably, also, the injured muscle-tissue shares in the formation of both the provisional and the definitive callus, always through the intermediate stages of medullary

tissue. The newly formed trabeculæ of bone are in every respect identical to those observed after plastic periostitis, and in this situation termed "exostoses" and "osteophytes." (See Fig. 164.)

The connection between the old and the new bone is established at the fractured surfaces by direct inosculation. At the surface of the compact bone, however, bay-like excavations are often wanting, and the newly formed bone may be attached to the old bone without the latter exhibiting any marked inflammatory changes. This occurrence has misled some authors into the belief that the newly formed bone is simply in apposition to the compact structure of the old bone, without being directly connected with it. Such views must be the result of the study of dry specimens, for in all other preparations there is no difficulty in ascertaining a direct union of the newly formed bone-corpuscles with the old ones by means of anastomosing offshoots.

The originally irregular and bulky new formation of bone, gradually—viz.: after several months—is transformed into a more regular osseous structure. This can be explained by the supposition of repeated dissolution and new formation of bone-tissue only. After the lapse of several years the bony cicatrix becomes so perfect, and even supplied with a central marrow-space, in continuity with the old one, that, were it not for the deviation of the fractured ends, no trace of the former accident could be discovered.

My researches may be summed up in the following statements:

(1) The injury done to the bone and the adjacent soft tissues by the fracture leads to an inflammation, which is most intense in the most vascularized tissue—viz., in the periosteum;

(2) The inflammatory new formation results in the production of a medullary or inflammatory tissue, from which arises cartilage tissue, representing the formation termed "provisional callus";

(3) The cartilage tissue at certain regular intervals, which depend upon the new formation of blood-vessels, is broken down into a freely vascularized medullary tissue;

(4) The medullary tissue, which has sprung from the former cartilage, produces bone, first in the form of irregular trabeculæ, constituting the formation termed "definitive callus";

(5) The formation of the definitive callus is in all essentials like the formation of bone in the process of normal ossification from cartilage and periosteum.

NECROSIS. BY C. F. W. BÖDECKER, OF NEW YORK.*

The successful study of the elements of bone-tissue depends very much upon the method employed. The proper examination of bone-tissue originated in the second, third, and fourth decade of this century, and was pursued by Howship, J. Müller, Henle, and others; all of whom resorted to dry bone, which they divided into thin slabs by the use of the saw, after which these were ground thin by a variety of devices, reducing each specimen to semi-transparency. Observations made in this way resulted in the theory of canaliculi bearing a solution of lime-salts. In 1850 and 1853, Rodolph Virchow and F. C. Donders applied the cell doctrine of Schwann to the explanation of bone-tissue. They sometimes used dry and sometimes fresh bone in their investigations, macerating it in dilute hydrochloric acid, whereby they liberated the elements of the structure more or less distinctly. The bodies so isolated presented, sometimes, nucleated structures connected together by branches; at other times, completely isolated bodies consisting of a central mass with projecting processes, and to these they gave the name bone-cells. Donders drew attention to the fact that bone-tissue had spaces filled by cell-like structures similar to those of other kinds of connective tissue. E. Neumann, in 1863, asserted that the so-called bone-cells were not the cells designated by Schwann, but spaces with offshoots having a more densely calcified wall than the other basis-substance, and thus better able to withstand the re-action of solvents. These bone-cells are no other than the lacunæ, and their offshoots, the canaliculi. Inasmuch as the dry method of examination of bone-tissue prevailed up to the introduction of the wet method, by Heinrich Müller, in 1856, it is not surprising that it is frequently persisted in to this day. The nearer to the living state the examinations can be made, the more instructive and definite will the observation be. Hence the dry method is fast falling into disuse among those making histological researches. In 1871, E. Lang introduced the examination of living bone under the microscope upon the heated stage, by which he noticed amœboid motion in bone-corpuscles. By this management the lacunæ were proved to contain protoplasm, but the nature of the contents of canaliculi he said nothing about. The method of examining bone-structure introduced by H. Müller—viz., to decalcify bone by the use of a solution of chromic acid—is to be preferred. In this way bones are decalcified in a short time, and without considerable change. For thin bones, two or three weeks are sufficient to soften them enough to produce sections of any degree of thinness by the use of the razor. Such sections may be stained by placing them in a solution of chloride of gold, of one-half per cent. in strength. An examination of such preparations will show that, within the lacunæ of the bone, nucleated bodies are to be seen, with finely granular offshoots extending into the larger canaliculi, where they are lost to sight. From the surface of the bioplasson body in the direction of the basis-substance many conical processes protrude toward the small canaliculi, with which they blend. In 1872, C. Heitzmann described and illustrated a bone-corpuscle from bone in the early stage of inflammation [see page 126, Fig. 40, of this book]. This figure shows very

* Abstract from "Necrosis," by C. F. W. Bödecker, D. D. S., M. D. S., New York. "Dental Cosmos," Philadelphia, 1878. In order to establish uniformity throughout the book, the term "protoplasm" is changed into that of "bioplasson."

plainly the shining, nearly homogeneous-looking bone-corpuscle, with offshoots in every direction, filling the whole caliber of the canaliculi. It solves the question of the contents of the canaliculi in bone by direct observation. The living matter in bone behaves precisely as in other tissues under the influence of the inflammatory process — that is to say, the central mass becomes a shining and nearly homogeneous lump, the offshoots from which occupy the whole caliber of the canaliculi, and by this the analogy of bone to all other varieties of connective tissue is established. That is to say, here, as elsewhere, the living part of the bioplasson *forms* a continuous net-work throughout the whole animal body, in the meshes of which a more or less fluid basis-substance is found, differing in its chemical properties in different situations, which in bone is glue-giving, and infiltrated with lime-salts.

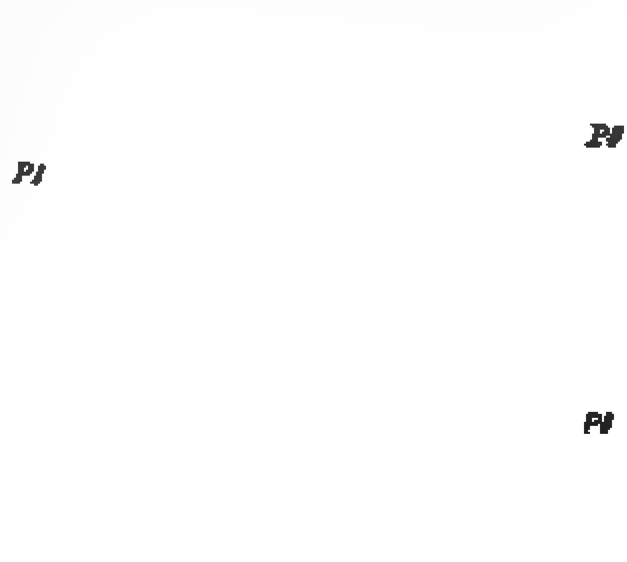


Fig. 165.— Normal Bone-tissue of the Lower Jaw of a Man, Aged Thirty Years. Chromic Acid Specimen, Stained with Chloride of Gold.

Three bone-corpuscles, P^1, with an oblong nucleus, P^2, with a globular nucleus, both exhibiting indistinct nucleoli, P^3, with a small, compact nucleus. Magnified 1000 diameters.

I have followed the methods, in my examination of bone tissue, as above described. This enabled me, by the use of the razor, to obtain sections fit to be examined by an immersion lens magnifying 800 to 1000 diameters. I noticed that the canaliculi could be plainly seen in sections, the basis-substance of which had retained a small quantity of lime-salts; in completely decalcified specimens they are very faintly discernible. According to my experience, it is better to stain the sections with a solution of chloride of gold of the half of one per cent., whereby a better view of both bioplasson and basis-substance is obtained. Another good way is to stain the sections with carmine and hæmatoxylon.

The results of my observations with high magnifying powers are that bone-tissue presents faint parallel lines, dividing it into the so-called lamellæ, within which we find the bone-corpuscles, the shapes of which vary according to the direction of the cut and of the lamellæ. As bone-corpuscles are flattened lenticular bodies, we will recognize them in this shape in the front view only. Longitudinal sections through these bodies give a spindle-shaped outline, small when cut near the boundary, broad when cut through the middle line of the lentil. A cross-section through a bone-corpuscle shows a somewhat irregular body. A cross-section from the compact bone of a lower jaw presents invariably bone-corpuscles in all three varieties. (See Fig. 165.)

We see large spaces, showing a number of ray-shaped offshoots. Besides these coarse offshoots, innumerable extremely fine light ones are present. The larger as well as the smaller all communicate with each other, forming a delicate net-work through the whole of the basis-substance. Within the lacunæ are present "protoplasmic" bodies. We observe, in the centers, shining oblong nuclei and nucleoli. Around the nuclei we see a narrow seam, trav-

ersed by numerous very fine threads, which are cone-shaped. Their bases are directed toward the nucleus, from the periphery of which they arise, while their points are in connection with the nearest granules of the protoplasm. Within the corpuscle there are finer and coarser granules, all being connected with each other by very fine threads. The seam around the nucleus, as well as the spaces between the meshes of the threads, are observable, being much lighter than the latter.

From the periphery of the bioplasson body numerous thick offshoots enter the larger canaliculi, which sometimes can be followed up until they communicate with the bioplasson of other large neighboring canaliculi. Besides these, many very fine offshoots run from the periphery of the bioplasson, contained in the larger canaliculi towards the basis-substance. Some of them can be seen to enter the fine canaliculi, but their course cannot be distinctly followed. My preparations show a much finer net-work within the basis-substance than Heitzmann's figure, before alluded to. Though I am not able to distinctly demonstrate the presence of living matter in the finest canaliculi, yet, as we find it in all other kinds of connective tissue, I am justified in assuming it. In normal bone, the lacunæ and canaliculi are not entirely filled by the living matter. On the periphery of each corpuscle we see a distinct light seam, traversed by the offshoots, which, in a cross section, only show the bioplasson in the center of the canaliculis, hence leaving sufficient space for the nutrient circulation.

It is impossible to study the differences between necrotic and normal bone if the specimens be prepared from dry osseous tissue.

I have made microscopical examinations of necrotic bone from the lower jaw, and from another piece from an upper jaw removed by Dr. Frank Abbott. The methods employed were exactly the same as before described from normal bone. In both cases the necrotic sequestra, as soon as they had been taken from the mouth, were placed into the solution of chromic acid, and cut in due time. As these pieces were small, I imbedded them in a mixture of paraffine and wax (after the extraction of the water by treatment with alcohol for twenty-four hours), whereby I was enabled to obtain extremely thin sections, some of which I stained with chloride of gold, some with hæmatoxylon, and some I mounted unstained.

The results of these examinations were as follows:

The outer surface of the necrotic bone, which, to the naked eye, looked rough and eaten out, when brought under the microscope showed bay-like excavations, known formerly as "Howship's lacunæ," in which there was visible a granular mass mixed with pus-corpuscles. In the middle of the bone I found all the Haversian canals more or less enlarged, some showing the bay-like excavations. The contents of the Haversian canals were everywhere the same — a conglomerate mass of darkly shaded granules, which I was unable to stain with carmine. These masses are the same that we see in decomposition of organic matter—"micrococci." Here and there some medullary corpuscles and multinuclear bodies were recognizable. I did not see blood-vessels in any of the Haversian canals. In the necrotic bone I found the traces of former osteitis. The enlargement of the Haversian canals and lacunæ are direct proofs of this; the dissolving out of the basis-substance on the periphery may, on the contrary, have been due to chemical changes, produced by infiltrations from the neighboring inflamed tissues. The Haversian systems and concentric lamellæ were unchanged. The lacunæ and canaliculi were yet preserved. In the necrotic preparation from the lower jaw I observed many

lacunæ in which the bioplasson body, with its net-work, was yet distinguishable, especially where the sequestrum had been attached to the periosteum. I found, also, in the preparation from the upper jaw, some comparatively unchanged bone-corpuscles.* But the majority of the bone-corpuscles, and especially in the neighborhood of the Haversian canals, were either empty or their bioplasson bodies were shriveled up (probably the remains of the living matter), only showing a few coarse granules. (See Fig. 166.) No signs of fatty degeneration could be seen, for the granules were stained violet by chloride of gold. Many lacunæ showed no structure at all, the contents looking rather like a mass of coagulated albumen. In none of these lacunæ was the characteristic structure of bioplasson recognizable.

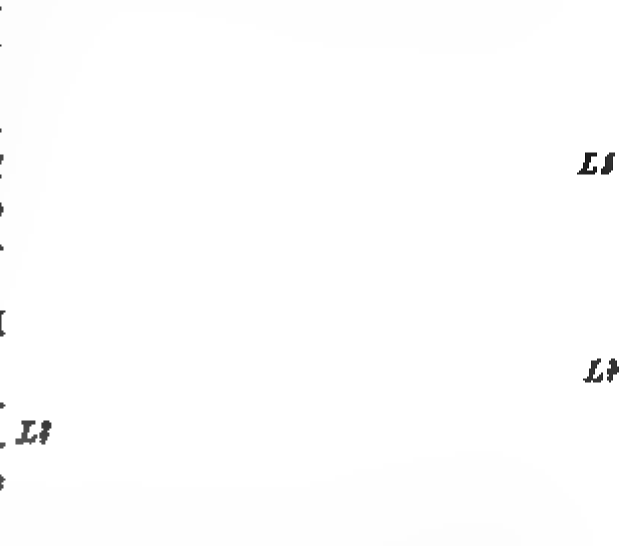


FIG. 166.—NECROTIC BONE-TISSUE OF THE LOWER JAW OF A WOMAN, AGED THIRTY-EIGHT YEARS. CHROMIC ACID SPECIMEN, STAINED WITH CHLORIDE OF GOLD.

Three lacunæ: L^1, with two clusters of a granular mass; L^2, with scanty granules; L^3, with a nearly homogeneous mass. Magnified 1000 diameters.

To sum up my observations, I found:

First. The lacunæ contain a bioplasson body, with a distinctly visible net-like arrangement, to be regarded as the living matter proper.

Second. The basis-substance is pierced by numerous coarse and fine canaliculi, communicating with each other, as well as with the lacunæ.

Third. The bioplasson bodies, which do not quite fill the lacunæ, send offshoots of the living substance into the canaliculi, but can only be seen in the coarser ones.

Fourth. In necrotic bone, traces of former osteitis are visible, but no blood-vessels present in the Haversian canals, which are filled with micrococci.

Fifth. In necrotic bone, most of the lacunæ contain no bioplasson, but either a coarsely granular or a structureless mass—remnants of the living matter and coagulated albumen.

RACHITIS AND OSTEOMALACIA.

During the years of 1872 and 1873, I made a number of experiments, for the purpose of elucidating the causes of rachitis and osteomalacia. The results of these tedious and expensive experiments I published in 1873, in the form of a provisional communication.†

* An important feature is not mentioned in this article—viz.: that even in apparently unchanged bone-corpuscles the nuclei were jagged, as if shriveled, this sufficiently indicating death of bioplasson.—ED.

† Anzeiger der Akademie d. Wissensch. in Wien, 19 Juni, 1873, und Vortrag in der Gesellschaft d. Aerzte in Wien, October, 1873.

Marchand, Ragsky, Lehman, Simon, and others, found free *lactic acid* in the urine of persons affected with either rachitis or osteomalacia. C. Schmidt discovered lactic acid in the liquid of malacic shaft-bones which had been transformed into globular cysts. Based upon these researches I commenced, in April, 1872, a series of experiments on the influence of internal administration and subcutaneous injection of *lactic acid on the bones of living animals.* These experiments were continued till the end of October, 1873, and were made on five dogs, seven cats, two rabbits, and one squirrel.

The result was that in dogs and cats, in the second week of the administration of lactic acid, no matter whether introduced with the food or by subcutaneous injection, the quantity of lime-salts given with food being simultaneously reduced, swellings appeared in the epiphyses of the shaft-bones of the extremities, and at the insertions of the rib-bones into their cartilages. The enlargement of the epiphyses and the ribs increased continually up to the fourth and fifth week, and at the same time curvatures of the bones of the extremities were noticed. Catarrhal inflammation of the conjunctiva, the bronchi, the stomach, and the intestines, emaciation and twitching of the extremities, were the concomitant symptoms.

The microscopical examination of the epiphyses demonstrated the identity of this pathological process with that seen in the epiphyses of rachitic children.

On continuing the administration of lactic acid, the enlargement of the epiphyses of the long-bones decreased, and the shafts themselves became, to a certain degree, less curved, while catarrhal inflammations of the mucous membranes occurred repeatedly. After four or five months, softening of the shaft-bones set in to such a degree as to render the bones as pliable as willow-boughs. The microscopical examination of the bones, after administration of lactic acid, continued for four to eleven months, showed a condition of things identical to that seen in human beings, dead of osteomalacia.

In the three herbivorous animals no swelling of the epiphyses was observable. One rabbit died in the third month, the other in the fifth month, of the administration of lactic acid, both having symptoms of inanition. In the bones of these animals there were no marked signs of rachitis or malacia. The squirrel, on the contrary, which died after thirteen months' treatment with lactic acid, exhibited, in a high degree, the characteristics of osteomalacia.

From these experiments it follows that we are able to produce artificially in carnivorous animals, by continued administration of lactic acid, first, rachitis, and afterward osteomalacia; while in herbivora the same agent produces osteomalacia without a preliminary rachitic stage.

Thus, the identity of these forms of disease is demonstrated, and the differences in their course depend mainly upon the difference in the age of the animals in which the solution of the lime-salts is produced.

In October, 1873, I exhibited to the Society of Physicians, in Vienna, a female fœtus of seven months, which had died immediately after birth. The mother of this fœtus had been employed by me for months to feed the animals with lactic acid. In this fœtus the symptoms of congenital rachitis were in the highest degree marked, to such an extent that the skull-bones were entirely absent, the cartilages of the ribs and the extremities showed only scanty depositions of lime-salts, but numerous breaches in the continuity; and throughout the body of the otherwise well-developed fœtus there could be found no trace of bone-tissue.

Feeding with lactic acid was repeated by E. Heiss,* on a dog one year and six months old, with only negative result. The age of dogs and cats in which rachitis can be induced is between the first and six months of life—at the period, therefore, when the skeleton is developing from the cartilage and the periosteum. After this stage of development is passed, the symptoms of osteomalacia will be produced, and with greater certainty, toward the end of the first year of the animal's life. The experiments of Heiss rest on mistaken grounds. Age is an essential factor in the production of either of these diseases in human beings. Rickets occurs only in children between the first and the fifth years of life, this corresponding with the age of the above-named animals. Osteomalacia is exclusively a disease of adults.

Rachitis (Rickets). This disease of early childhood in its clinical features has been well known for over two centuries.

Whistler† was the first to describe it, and from the title of his book the name of "English disease" was adopted by the German physicians. Next followed G. Glisson,‡ who made use of the name "rhachitis."

Simon,§ according to Marchand and Lehman, found lactic acid in the urine

* "Zeitschr. f. Biologie," Bd. xii.

† "De Morbo Puerorum Anglorum," 1645. Rare book.

‡ "Tractatus de Rhachitide," 1659.

§ Lehrbuch d. Med. Chemie., 1842. Bd. ii., p. 203.

of rachitic children. He says that such children void urine which sometimes is very rich in lactic, also in oxalic, acid, and that it contains four times as much phosphate of lime as the normal urine of children. Rickets may be caused by the formation of lactic acid in the digestive tracts; certainly this acid is not disposed of in the blood, in which only a small portion of the nitrogenous material is transformed into urea. In osteomalacia of adults, the lactic acid in the urine is considerably augmented, as well as the uric acid. In rickets, the lactic acid dissolves the phosphate of lime of the bones, and these become pliable; while, in osteomalacia, even the organic portion of the bone is in part absorbed.

G. O. Rees* gives a thorough chemical analysis of the earthy phosphates in "Mollities ossium." He found the resorption of the phosphates to be different in different bones, and in the softened bones, on an average, he found only 78 per cent. of the normal 86 per cent. of phosphate of lime. The absorption, he says, affects the carbonate less than it does the phosphate of lime.

Chossat † observed the absorption of lime-salts in pigeons which had been fed exclusively on wheat. The "rarefaction," of bone corresponds more closely with osteomalacia than it does with rickets. Diarrhœa was a concomitant symptom of this disease. Sam. Solly ‡ distinguishes two varieties of softening of bone. Osteomalacia, he says, has also been observed in animals by Spooner, especially in dogs, with post-mortem results identical with those found in man. Sometimes the disease is confined to single bones.

C. Schmidt § found the lactic acid by combining it with zinc, in the acid liquid of cysts into which the malacic bones were transformed, and he thought that the lactic acid was of local origin. Ernst V. Bibra ‖ observed, in accordance with the experiments of Chossat, that by withdrawing the lime-salts from fowls the lime-depositions in the egg-shell disappeared, and finally the fowls ceased laying eggs altogether. The bones of chickens showed a decrease of about 10 per cent. of the inorganic substances and a decrease of 6 to 10 per cent. of the phosphate of lime; while the carbonate of lime and phosphate of magnesia were only a little lessened, and the alkalies and the fat not at all. V. Bibra found no lactic acid in fresh bones; no consideration is given to this acid in his chemical analyses.

J. Schlossberger ¶ obtained the following results: In the normal occipital bone the percentage of inorganic material never falls below 60 per cent. In craniotabes the percentage sinks to 51–53 per cent., and in the spongy and thickened portions to 43–48 per cent. Carbonate of lime is either decreased or normal.

Guérin[1] says that if young animals are given other food than milk, disturbances of nutrition, especially of the bones, will follow. He took pups of the same litter, and fed some with exclusively animal and others with mixed vegetable food (bread and milk). The latter remained healthy; the former

* Guy's Hosp. Reports, viii., p. 191. Schmidt's Jahrb., 1841.
† Comptes rendus. Tom. xiv., p. 451–454.
‡ Med.-Chir. Transactions, xxvii. 2d Ser., ix., 1844.
§ Annales de Chem. et Pharm., lxi., 3, 1847.
‖ "Chem. Untersuch. über die Knochen u. Zähne des Menschen u. der Wirbelthiere." Schweinfurt, 1844.
¶ "Chemische Untersuchungen über d. erweichten Kinderschädel." R. u. W. Arch. viii. Schmidt's Jahrb., 1849, Bd. lxii., p. 277.
1 *Gazette des Hôpitaux*, xxxvii., 1848.

at first grew rapidly, but soon diarrhœa set in, they emaciated and became rachitic. The bones became so soft that the animals walked on their femurs and humeri, which were very much curved. The main cause of rachitis, according to this author, is animal food, given too early.

G. Wegener * made experiments on fowls and calves, producing rachitic changes by the administration of small doses of phosphorus, continued for months. He found the epiphyseal cartilage considerably dissolved out, and also in a high degree of hyperæmia.

The histology of rachitic bones has been studied by many excellent observers, such as H. Meyer, R. Virchow, H. Müller, A. Kölliker, C. Wedl, Steudener, and others. H. Meyer † especially comes to the conclusion that: (1) osteomalacia is osteoporosis; (2) rachitis originates from universal periostitis; (3) osteomalacia and rachitis are the consequences of one and the same disease.

We know that, in the normal process of ossification, both cartilage and periosteum are reduced to a juvenile condition, giving rise to medullary tissue. Simultaneously, also, new red blood-corpuscles and blood-vessels are formed. *In rickets, all this is going on in a more rapid manner, but the new formation of bone from the medullary tissue is very scanty or entirely absent.*

In sagittal sections of the epiphyseal ends of rachitic bones we notice an intensely yellowish-red zone on a level with the portions in which the formation of medullary tissue from cartilage is going on, and we see that this portion is considerably thickened, constituting the characteristic rachitic swelling of the shaft-bones. Under the microscope we find, at the level mentioned above, large cartilage corpuscles containing a far greater amount of bioplasson than normal. The calcification of cartilage is scanty and in irregular patches, or sometimes completely wanting. The large, irregular, newly formed medullary spaces abound in hollow, club-shaped formations—the future capillaries—which contain numerous hæmatoblasts and red blood-corpuscles. At the peripheral portions of the epiphyseal cartilage a *new formation of vascularized cartilage*, instead of bone, can be traced, while the newly formed trabeculæ of bone are scanty, irregular in shape, holding large bone-corpuscles and territories with distinct boundary lines. Similar features are observed at the points of junction of hyaline cartilage and bone in rachitic ribs. Here, too, the new formation of cartilage is proceeding from medullary tissue on a large scale, mostly in groups, representing the territories. The cartilage is dissolved out, leaving a

* Virchow's Archiv, Bd. lvi.
† "Zur Lehre von den Knochenkrankeiten." Henle u. Pfeiffer's Zeitschr., iii., 1853.

medullary tissue freely supplied with blood-vessels of considerable caliber, venous and capillary chiefly; but the production of bone from this vascularized tissue is extremely scanty and without uniformity. (See Fig. 167.)

At the peripheral portions of the shaft-bones we find, between the thin cortical bone-tissue and the fibrous portion of the periosteum, a broad layer of medullary tissue, which is sometimes arranged in patches. The blood supply of this medullary tissue is so great as to give the appearance of a hemorrhage to the

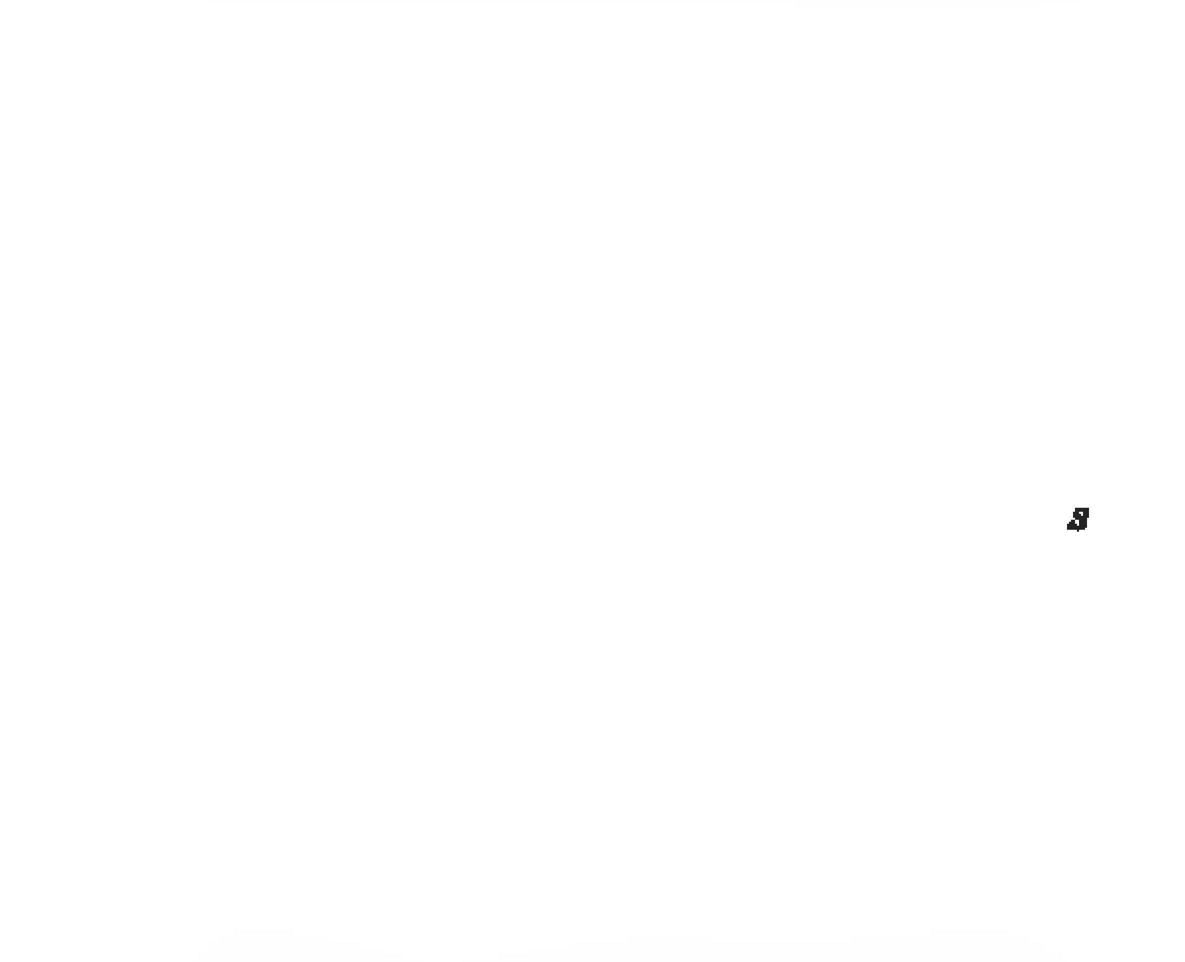


Fig. 167.—Rachitis. Rib of a Child, in Tranverse Section. Chromic Acid Specimen.

C, cartilage corpuscles, arranged in territories; *MS*, medullary space, sprung from cartilage tissue; *M*, medullary tissue with very large blood-vessels, *BV*, and a scanty new formation of bone-tissue, *B*. Magnified 200 diameters.

naked eye. The bone generally remains in the stage of cancellous structure, with large, irregular medullary spaces.

The flat skull-bones, being developed from fibrous connective tissue, exhibit similar features—the so-called *craniotabes*. In some places medullary tissue is formed, leading to a reproduction of fibrous connective tissue, instead of bone; or already formed bone, through the intermediate medullary stage, passes into a

new formation of fibrous connective tissue, resulting in thinning of the bone. In other places the exuberant growth of medullary tissue causes a broadening of the diameter of the bone, with a scanty trabecular new formation of bone-tissue. Both the medullary and the newly formed connective tissue are supplied with a considerably larger amount of blood-vessels than is seen in the normal condition.

The pathological condition is that of a plastic inflammation, in accordance with the views expressed by Virchow, and there is good reason to consider the process of rachitis as an inflammation.

By feeding pups and kittens with lactic acid, rickets was induced, exhibiting in the osseous system features identical to those observed in rachitic children.

Osteomalacia. This rare form of disease, which is always accompanied by intense pains, usually attacks the vertebral column and the pelvic bones, though there are cases on record in which the whole skeleton was rendered as pliable as wax.

Under the microscope we see a decalcification of fully formed bone-structure, usually of the compact portions, advancing in a way similar to the inflammatory process. The bone-tissue is transformed into medullary tissue, which in some places is distinguished by a large quantity of blood-vessels. My researches enable me to state that the ultimate productions from medullary tissue are of two kinds: either colloid globules or simply fibrous connective tissue.

In a femur of a woman who, during pregnancy, was attacked with osteomalacia, and died of the disease, the compact portion of the bone was reduced to the thinness of a pasteboard, and was very pliable. The central marrow space was filled with a smeary, grayish yellow mass, which, under the microscope, proved to be colloid—viz.: consisted of globular or irregularly shaped corpuscles of a luster similar to fat, but not yielding to the re-agents which dissolve fat. They resisted even the action of strong alkalies and acids which destroyed the bone-tissue proper, and assumed a dark purplish violet color upon being stained with chloride of gold. (Fat is unaffected by chloride of gold.) Within the globules radiating bodies were often seen, somewhat similar to the needle-shaped crystals of the so-called margaric acid. Between the globules scanty fibrous connective tissue with a few blood-vessels was noticeable.

The origin of the colloid corpuscles could be traced in the thin compact shell of the femur, in which the lamellæ were much

more marked than normal, evidently due to a dissolution of the lime-salts during life. Numerous medullary spaces, containing a varying number of colloid corpuscles, traversed the bone. Some of these bodies exhibited faint traces of the medullary corpuscles which composed them; others, in the initial stage of the colloid metamorphosis, were distinctly seen, consisting of medullary corpuscles, so that each colloid body might be considered as having originated from a group of coalesced medullary corpuscles. In some places long rows of colloid corpuscles were noticeable, each of which resembled a territory with a condensed, peripheral colloid frame, and a central body, somewhat like a bone-corpuscle. (See Fig. 168.)

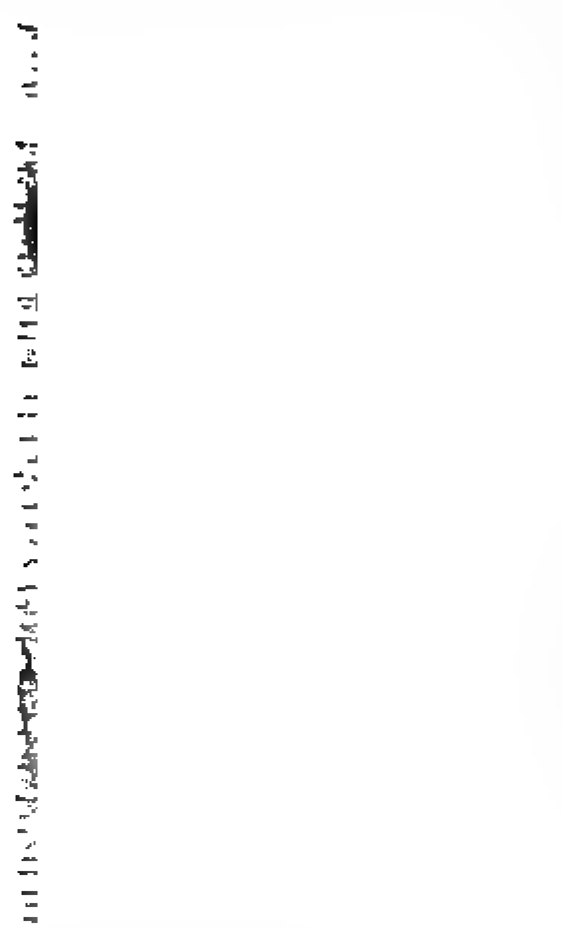


Fig. 168.—Osteomalacia. Femur of a Woman; Longitudinal Section. Chromic Acid Specimen.

B, bone-corpuscle; *L*, distinctly marked lamellæ; *C*, colloid corpuscles, arranged in a row. Magnified 500 diameters.

In the rib-bone of another woman, dead of osteomalacia, I found very large medullary spaces, which were filled partly with medullary and partly with fibrous tissue, and contained also a number of yellow-brown pigment clusters. These spaces were very vascular. In this case no colloid corpuscles could be detected.

In dogs and cats, whose bones were artificially brought into the condition of osteomalacia, all features described above as occurring in the malacic femur of the woman were present, and especially the colloid globules. These closely resemble fat-globules, but, nevertheless, were an entirely different substance, as they did not yield to strong alkalies and acids, not even after being boiled with them. Chloride of gold stained them a dark purplish-violet color. The bones of the squirrel, which had been fed for thirteen months with lactic acid, had compact portions as thin as paper. They were, to a great extent, transformed into medullary and fibrous tissue; they contained a large number of blood-vessels

and pigment clusters, but no colloid corpuscles. The resemblance the case bore to the second case of malacic ribs was very striking.

In conclusion, I wish to say a few words as to the withholding of lime food in the animals experimented upon. It was, in fact, only a reduction, but not by any means an entire cutting off of the lime supply. The dogs and cats were fed with fresh boiled meat, with fat, with milk and white bread; but no bones were given. The desire of all these animals for lime food, during the treatment with lactic acid, was evident. The cats and dogs rushed for egg-shells, whenever they came within their reach; the squirrel scraped off the kalsomining from the wall so eagerly that its cage had to be removed from the wall, though its food was that suitable for squirrels.

In a dog, in which osteomalacia had been induced, I produced a subcutaneous fracture of the leg-bones. When the animal was killed, seven weeks after the fracture, the callus exhibited a marked cartilaginous new formation, but with only a scanty deposition of lime-salts and very limited new formation of bone near the injured bone-tissue. As in the above-named period the fractured bones of normal dogs invariably exhibited the formation of a defined cancellous bone-callus, in the dog treated with lactic acid the formation of a bone-callus was obviously prevented.

As to the case of the seven months fœtus, completely destitute of bones, born of a woman who for months during her pregnancy had fed the animals with lactic acid, I wish to state that this woman must certainly have inhaled the vapors of lactic acid, more particularly if poured into the warm soup destined for the animals. The woman was otherwise healthy, and remained so after delivery; nevertheless, it must be mentioned that, several years previously, she had given birth to a child which in early childhood was slightly rachitic. The seven months fœtus died of cerebral hemorrhage, which had evidently taken place during delivery, as the protecting skull-bones were absent.

2. Inflammation of Muscle. Trichinosis.

In 1868,* I published a series of observations and experiments leading to the conclusion that the villi of the small intestine had, at their points, perforations which opened directly into the central lymph-vessel of the villus. The existence of these openings could not, however, be positively proved. If these were really an anatomical condition, we could easily understand how the embryo trichinæ are transported from the cavity of the small intestine, first into the chyliferous duct and afterward into the vascular system. The trichinæ could be carried with the blood, and fixed

* "Zur Kenntniss der Dünndarmzotten." Sitzungsber. d. Wiener Akademie d. Wissensch., lviii., Bd. 1868.

as emboli in the tissue of striped muscles, at the points where the arteries merge into capillaries, which, owing to their rectangular division (see page 274, fig. 117), would retain the worms. Muscles which have a continuous motion and a markedly rectangular division of their blood-vessels — f. i., the diaphragm — would be the first to be invaded by the parasites, while muscles without this rectangular arrangement of the vessels—f. i., the heart—would not be apt to become trichinosed.

The theory that the trichina embryos perforate the walls of the intestine, and thence migrate into the muscles, is highly improbable, as these parasites have no apparatus for perforating tissues.

At the time before mentioned, I made in the Vienna Veterinary School a number of experiments for the purpose of observing trichinæ in the chyliferous system of the intestine. I fed Guinea pigs with fresh trichinosed muscle; but these experiments proved to be failures, as the animals became so rapidly affected after a few days that all of them died, and I looked in vain for embryonal trichinæ in the villosities of their small intestines.

As soon as the embryos of trichinæ reach the muscle an inflammation of this tissue (myositis) sets in, which I have studied in all its phases.

As to inflammatory changes of *smooth muscle*, we know, through the researches of Durante and others, that the spindles divide into rows of inflammatory corpuscles, which at first retain the general shape of the original muscle-spindles. Later, the corpuscles break apart in the same way as those sprung from connective tissue.

Inflammation of the *striped muscles* has, since 1851, often been the subject of microscopic researches. Some observers have asserted that only the nuclei of the muscle-fibers participate in the inflammatory new formation; others, that both the nuclei and the contractile substance proliferate; again, others have denied any participation of nuclei or contractile substance, believing that both perish, and that the whole inflammatory new formation is due only to an emigration of colorless blood-corpuscles. Colberg especially, in 1864 asserted that in trichinosed muscles an increase of the nuclei occurs. Spina, one of the recent writers on the inflammation of muscle, based his views upon researches made in the frog's tongue, which he had artificially inflamed; he claims that the nuclei become much augmented, and that the contractile

substance itself breaks up into pus-corpuscles, and that from solid caky masses, the product of the inflamed muscle tissue—red blood-corpuscles arise.*

The invasion of muscle-tissue is immediately followed by an inflammatory process, visible first in the perimysium. (See Fig. 169.) The perimysium becomes thickened and more or less crowded with inflammatory corpuscles. The basis-substance is liquefied, the tissue reduced to its juvenile condition, and the newly appearing medullary corpuscles by increase of their living matter become augmented in the same manner in which fibrous connective tissue in general is affected by the inflammatory process. (See page 356.)

The muscle-fibers in the earliest stages of inflammation are unaltered, but very soon a marked change takes place in certain portions, depending upon the location and number of the parasites. The process may attack single muscle-fibers in such a way that almost unchanged fibers lie close to those exhibiting highly advanced alterations in their texture; or even a single fiber may be normal in parts, and in parts invaded by the inflammatory process.

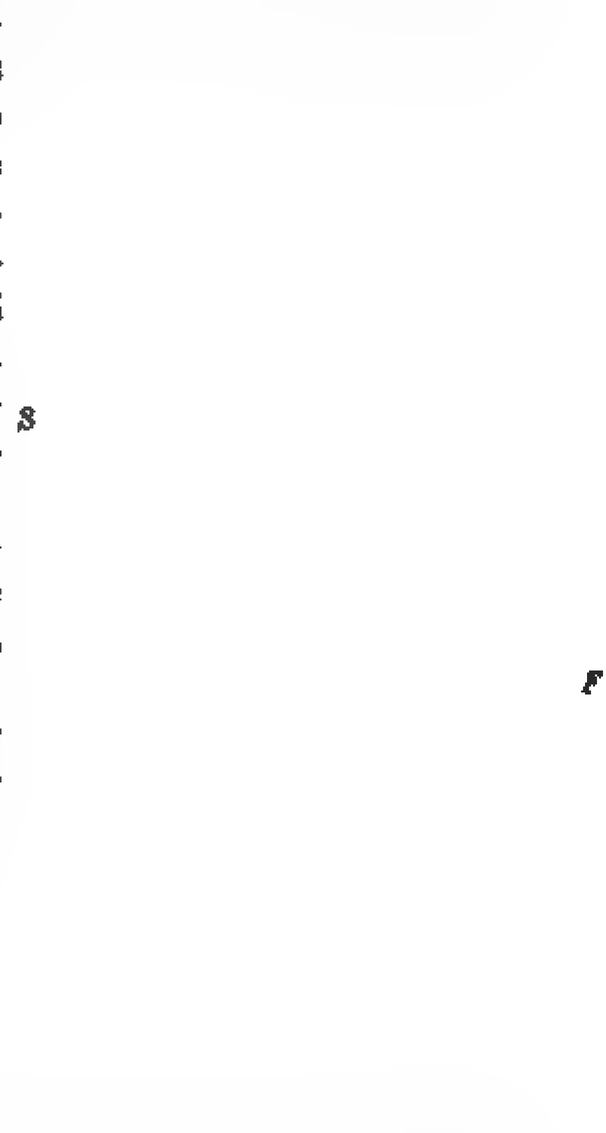


FIG. 169.—STRIPED MUSCLE FROM THE LEG OF A MAN, RECENTLY INVADED BY TRICHINÆ.

F, trichina in front view. *S*, trichina in side view. Magnified 200 diameters.

The first noticeable change consists in an enlargement of the sarcous elements and a destruction of their regular arrangement, together with the appearance of a larger number of bodies, usually termed the nuclei of the muscle-fiber. These formations

* Arnold Spina. "Untersuchungen über die entzündl. Veränderungen d. quergestreiften Muskelfasern." Wiener Mediz. Jahrbücher, 1878. In this essay a full account of the literature of this subject is found.

being present in the middle of every muscle-fiber as well as at its periphery, in both situations clusters of nuclei are found, some of which have originated from former nuclei, while others are newly formed. A division and multiplication of the nuclei is inferred from the fact that we frequently find clusters of nuclei, exhibiting cleavage, or marks of division.

The next change is that, by an increase of the bioplasson of the sarcous elements, solid lumps arise, which in turn are split into a reticulum and become nucleated, by the usual process of formation of reticular from solid bioplasson. Thus medullary or inflammatory corpuscles become visible, arranged in clusters, which are unquestionably identical with those embryonal formations from which the striated muscle-tissue is developed. Instead of clusters of medullary corpuscles, sometimes multinuclear bioplasson masses are observed. These clusters are separated from each other by rims broader than those between the single medullary elements; but all of these and all of the clusters remain uninterruptedly connected by means of delicate bioplasson filaments which traverse the interlying light rims. (See Fig. 170.)

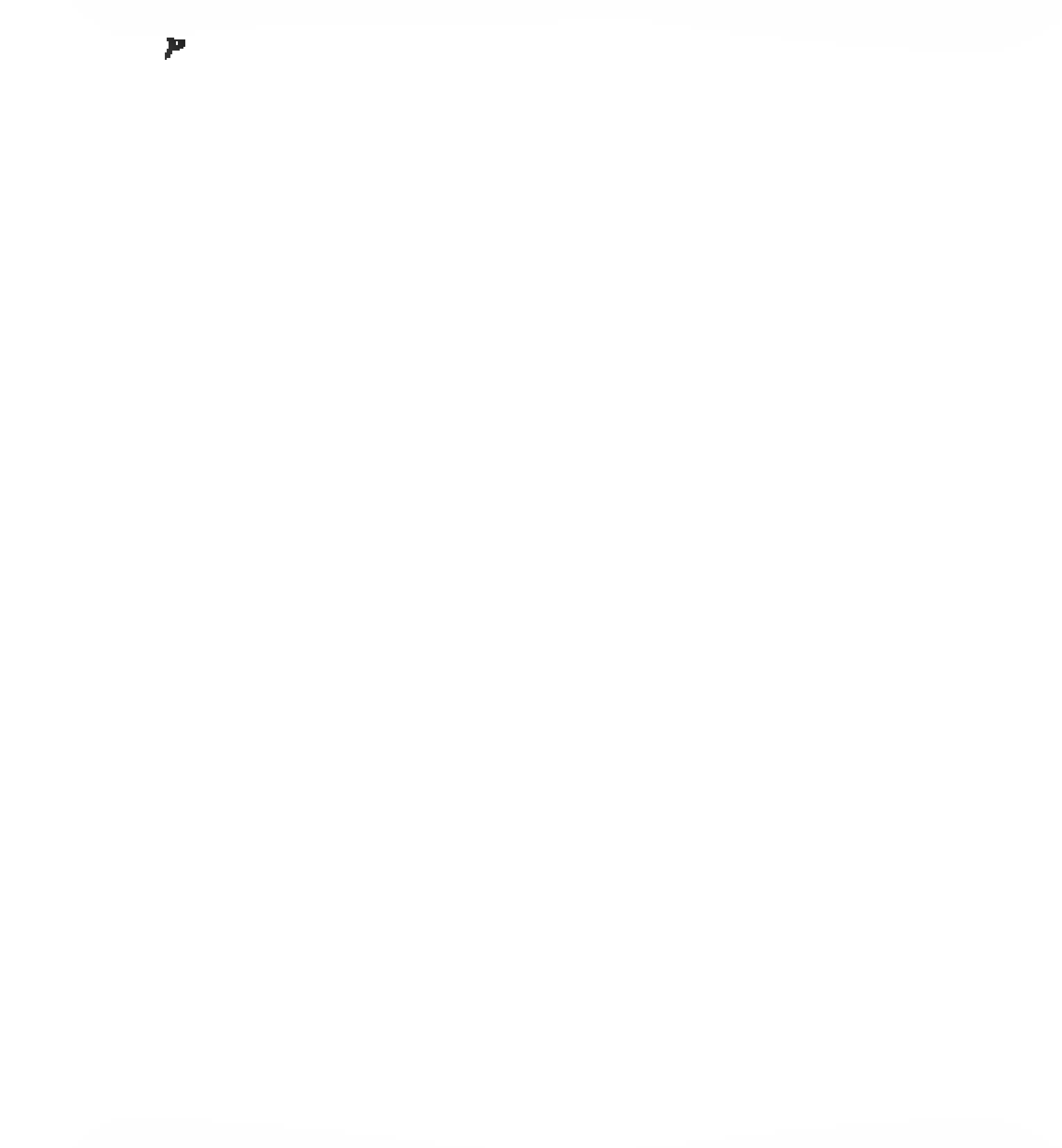
The clusters are arranged in rows, indicating that at first the sarcolemma remains unaltered. Afterward, however, it becomes liquefied, and the inflammatory corpuscles sprung from the muscle-tissue commingle with those produced by the perimysium, and in this manner more or less extensive masses of inflammatory corpuscles are formed, which are bounded by relatively little changed muscle-fibers.

A second change of the muscle-tissue consists in an enormous increase of the bioplasson of the sarcous elements, which, by confluence, produce irregular, caky, and globular masses of a high degree of luster, apparently destitute of structure and closely resembling fat. Former observers mistook these formations for the result of a degenerative process. According to Spina's view, which is undoubtedly correct, they are the products of a progressive inflammatory change of the contractile muscle-tissue.

These formations are not soluble in turpentine, therefore are not fat; they are readily stained with chloride of gold, but not with carmine. Evidently, they are solid lumps of bioplasson in a juvenile condition, which, in 1872, I termed "hæmatoblastic." From them originate, by division, a number of small solid particles, each of which gives rise to a new inflammatory element, or, should the lumps break apart and become isolated, to red blood-corpuscles. Such corpuscles are often found in clusters within

unbroken sarcolemma sheath, which plainly demonstrates t they are not the result of hemorrhage.

After the inflammation abates, the medullary corpuscles give to a more or less extensive new formation of connective tis-, constituting a cicatrix in the middle of the muscle. Clusters medullary corpuscles may again proceed to the forming of



170.—INFLAMMATORY CHANGES OF MUSCLE-TISSUE AFTER RECENT INVASION OF TRICHINÆ. FROM THE LEG OF A MAN.

M, inflamed perimysium. *P*, initial inflammatory change of muscle, *I*, high degree of mmatory change, *L*, homogeneous caky, and *F*, globular, masses of solid bioplasson, *C*, lary blood-vessel, with enlarged endothelia. Magnified 600 diameters.

iated muscle-tissue, as was first maintained by C. O. Weber. , on the contrary, the filaments connecting the inflammatory rpuscles break, pus-corpuscles will be produced, and by their

presence establish an intramuscular abscess. I have observed this result after amputation of the tongue, for cancer, with the galvano-cautery.

The cicatrix may, under certain conditions, become transformed into bone; and regular bone-plates are sometimes met with in muscle-tissue, which, for a long period of time, was exposed to irritation.

If, from the very beginning, the inflammatory process is confined to the perimysium, a hyperplasia of connective tissue will ensue, which is often mistaken for genuine hyperplasia of the muscle-tissue itself.

In trichinosis, one of the results of the plastic inflammation is the formation of a hyaline capsule around the parasite, provided that the life of the patient is sufficiently prolonged for such a comparatively favorable termination. How the capsule is formed I cannot say from direct observation. In old cases of trichinosis we find in the middle of the capsule one, sometimes two, worms, coiled up with the well-known two and a half turns, shriveled and evidently saturated with lime-salts. (See Fig. 171.)

The space between the trichina and its capsule is filled with a granular deposit of lime-salts. Such depositions are frequently met with at the poles of the capsule, and sometimes they have a peculiar stratified appearance. In the vicinity of an encysted trichina we always find cicatricial fibrous connective tissue replacing the muscle fibers which were destroyed by the former inflammatory process, and the cicatrix, as a rule, contains a varying number of fat-globules.

FIG. 171.—ENCYSTED TRICHINA IN THE PECTORAL MUSCLE OF A MAN.

T, shriveled trichina, surrounded by a granular calcareous mass and inclosed by a hyaline capsule, *C*, *K*, knob-like deposition of lime-salts at one pole of the capsule, *F*, vacuoled fat-globules. Magnified 200 diameters

3. Inflammation of Nerve-tissue.

Inflammation of nerve-tissue is characterized by occurrences very similar to those observed in inflammation of connective tissue. All varieties of nerve-tissue—the gray substance, the ganglionic elements, the medullated and non-medullated nerve-fibers—first break down into medullary corpuscles, identical with those which in embryonal development took part in the production of nerve-tissue.

The first step of the inflammatory changes in nerves, as in muscle-tissue, always starts in the supporting and accompanying connective tissue, which, being the carrier of blood-vessels, reacts most promptly to the irritation. Next follows the proliferation of inflammatory corpuscles arising from the nervous tissue, and the sum of the inflammatory new formation, so long as the continuity of the corpuscles remains unbroken, results in the production of a dense, indistinctly fibrous connective tissue, establishing the condition of *sclerosis* in the tissues of the nerve-centers. Later, shrinkage of the newly formed connective tissue causes retractions on the surface of the brain, which process H. Kundrat terms *porencephalitis.*

Should the inflammatory corpuscles break apart in the early stages of inflammation, the result will be a complete destruction of the tissue involved—*i. e.*, the formation of an abscess. The wall of the abscess, again, may be built up by newly formed connective tissue. Such a combination of a formative and destructive inflammatory process is well illustrated by the following article:

Microscopical Studies on Abscess of the Brain. By H. G. Beyer, M. D., P. A. Surgeon U. S. Navy.*

The subject of my studies is a brain, the history of which is published in the Transactions of the New York Pathological Society, vol. i., edited by John C. Peters, M. D.

At a meeting of this society, held on January 13, 1875, Dr. J. Lewis Smith presented a specimen with the history, which is briefly as follows:

"Maggie, aged two years and six months, seemed in good health, was plump and well developed. On the evening of December 5th, she ate her supper as usual, and was placed in her crib, apparently in perfect health. At 3 A. M. she was found in severe general ecclampsia. The general spasmodic

* "Journal of Nervous and Mental Disease," July, 1880. The essay is here reprinted in abstract. The term "protoplasm" is changed into that of "bioplasson."

movements continued with more or less violence till 1.30 P. M., and in the muscles of the neck somewhat longer.

"At about 6 P. M., I found her lying quiet, rather stupid, but easily aroused. Her vision was evidently good, and she was conscious; the pupils responded to light, and the direction of the eyes was normal; pulse 104; no cough; respiration and temperature normal. There was no apparent loss of motion of the muscles of the face, but the right arm and legs were paralyzed, though the palsy was not complete. The great toe flexed on tickling the sole of the foot, but the foot itself showed little or no motion; but on attempting to flex the leg, which was extended, some rigidity of the muscles was observed. At times, the patient produced slight movement of the thigh upon the trunk. I think, during the two or three days succeeding the convulsions, sensation in the right limbs was not entirely lost, though greatly enfeebled. Subsequently paralysis in the right limbs, both of the nerves of sensation and motion, became nearly or quite complete, and continued so until death. Nevertheless, tickling of the sole of the foot caused some movements of the great toe. On the left side, sensation and motion were perfect.

"December 9th. Has vomited to-day for first time; apparently sees well, and the appearance of the eyes is normal; has no retraction of the head or rigidity of the muscles of the neck, nor along the spine; pulse 96; temperature normal; lies quiet with eyes shut; is stupid and not particularly fretful when aroused; her bowels moved regularly.

"December 11th. Continued to vomit at intervals; pulse 68.

"December 16th. Pulse 80, temperature 100; vomited once yesterday, not to-day; lies in a constant doze.

"December 18th. Moans at times, as if in pain; pulse 180, temperature 100° F.

"December 19th. Pulse 180, temperature 103°; there is convergent strabismus, and her eyes have a wild, almost insane, look; but she can see, and grasped, hurriedly, a percussion hammer presented towards her. Paralysis of nerves of motion and sensation in the right extremities nearly complete; slight movement could still be induced in the great toe by titillation; the vomiting has ceased; tongue covered with a thick fur; movements of the bowels pretty regular; has a slight cough, such as is common in cerebral disease.

"December 22d. Lies quietly on her side in perpetual slumber, with eyes constantly shut; pulse 118, temperature 101½°; the bowels still moved nearly normally. The pupils, when exposed to the light, were seen to oscillate, but are constantly more dilated than in health; the urine passes freely. Has, at intervals, circumscribed flushing of the features.

"December 24th. Pulse intermittent; pupils dilated.

"December 25th. Died in profound stupor to-day, having lived nineteen days from the commencement of the malady.

"Autopsy. On removing the calvarium and dura mater, which presented no unusual appearance, the vessels of the pia mater were found rather more injected than common. The cerebro-spinal fluid was scanty, and the surface of the brain rather dry. The vertex of the left hemisphere was unusually prominent, rising perhaps half an inch higher than that of the opposite side. At the highest point, which was about one inch and a half from the median line, was a circular yellowish spot upon the surface of the brain, about one and a half inches in diameter. Pressure upon the spot, made lightly, com-

municated the sensation of a large cavity underneath, filled with liquid, and approaching to within two or three lines of the surface. There was no adhesion or exudation at that point; and the surface of the brain appeared entirely normal, except slight cloudiness of the pia mater at the base of the brain, a little posterior to the optic commissure. The incised surface of the brain, at a distance from the abscess, showed no increase of vascularity. The right hemisphere appeared in every way normal, except that its lateral ventricle was filled with pus, but not distended.

"On the left side, occupying the center of the hemisphere, was an abscess as large as the fist of a child of two years, extending from within two to three lines of the vertex, where its site corresponded with the yellow spot on the surface of the brain, to the roof of the lateral ventricle. Through this roof the abscess had burst, filling and distending the ventricle with pus, and thence making its way into the lateral ventricle of the right hemisphere. The whole amount of pus contained in the abscess and the two ventricles was perhaps two ounces.

"The walls of the left lateral ventricles were much softened, the upper part of the corpus striatum and thalamus opticus being nearly diffluent. The walls of the right lateral ventricle were slightly softened, but to a less depth. The parietes of the abscess, which extended from the roof of the ventricle to the vertex, as already stated, were indurated to the depth of one and a half lines, except at the base of the abscess, which corresponded with the roof of the ventricle, where softening had occurred. The spinal cord, so far as it could be examined from the cranial cavity, had the usual vascularity, but was slightly softened.

"The cause of the encephalitis from which the abscess resulted was obscure. The inflammation, so far as could be ascertained, was idiopathic. There was no history of otitis, which is one of the most frequent causes of cerebral abscess; nor of heart disease so as to produce embolism. It seems probable, since there was no fever till about the fourth day after the convulsions, that an abscess had primarily occurred in the hemisphere between the roof of the ventricle and the vertex—possibly some weeks previously. The bursting of this into the lateral ventricle, and the constitutional disturbance, inflammation, and softening to which these would inevitably give rise, affords sufficient explanation of the history of the case, after the commencement of the convulsions."

The specimen was kept in a very dilute solution of chromic acid for several months, after which time it was hardened in alcohol and imbedded in a mixture of paraffine and wax, whereby care was taken to enclose mainly the wall of the abscess and its immediate surroundings. Previous to the beginning of my studies, a certain number of sections had been made of the wall of the abscess itself, as well as from other parts of the brain, such as the cerebrum, the cerebellum, the medulla oblongata, and the gray matter. These sections everywhere had been found holding a large number of so-called amylaceous corpuscles, exhibiting all the characteristic chemical and morphological features of these formations. No other changes could be traced out, nor did the blood-vessels show any anomalous conditions, excepting the capillaries, which were found dilated and choked with blood-corpuscles within the inflammatory focus, as well as in its neighborhood.

I made a number of sections, both from the wall of the abscess and the surrounding portion of the brain, which sections embraced the gray matter of

the corpus striatum, thalamus opticus, the cortex of the left hemisphere, also the white substance of the same, which, as is evident from the history, was the seat of the abscess. The specimens thus obtained were stained, partly with an ammoniacal solution of carmine, partly, after thorough washing out with distilled water, with a one-half per cent. solution of chloride of gold. The different sections were mounted in glycerine, diluted with distilled water — this method of mounting, as experience teaches, being far superior to the method of mounting in Canada balsam or dammar varnish. While glycerine-mounted specimens, if taken from properly hardened material, keep almost any length of time, never losing their sharp and definite outlines of detail, Canada balsam specimens, on the contrary, very soon become so transparent that their minute details are completely lost to sight, and only the coarser formations remain distinguishable. Canada balsam specimens, therefore, are fit for lower powers of the microscope only; they are worthless for a power exceeding 400 diameters, or for any power intended to give a display of the

F

M

W

FIG. 172.—WALL OF AN ABSCESS OF THE BRAIN. TRANSVERSE SECTION.

F, layer of fibrous connective tissue with scanty blood vessels, bounding the abscess; *M*, layer of myxomatous connective tissue, with numerous capillary blood-vessels; *W*, white substance of the brain, with numerous large blood-vessels. Magnified 200 diameters.

more minute anatomical features. Our lack of knowledge of the minute pathological anatomy of the central nervous organization is mainly due to the method of mounting in Canada balsam.

The subject of these investigations will be treated under the four following heads, namely: Inflammatory changes of—

(1) Wall of abscess; (2) white substance; (3) non-medullated nerve-fibers; (4) gray substance.

(1) *Wall of Abscess.* Transverse sections through the wall of the abscess, which in different places varied in width from one to two millimeters, exhib-

ited the following characteristic features. (See Fig. 172.) A layer of fibrous connective tissue forms the boundary of the abscess, its innermost portion presenting a somewhat jagged appearance, due to a number of attached pus-corpuscles. The bundles of connective tissue in this situation were partly infiltrated with, partly transformed into, pus-corpuscles, and were arranged in the shape of rows, between which a scanty basis-substance was traceable. In their general direction, these rows corresponded to that of the bundles in the subjacent tissue stratum, which was built up by dense bundles of fibrous connective tissue in a more or less parallel course, and with but few decussations inclosing narrow, oblong spaces. These connective-tissue fibers held a large number of small spindle-shaped and a somewhat larger number of globular bioplasson bodies, the former representing what has been termed connective-tissue corpuscles, the latter inflammatory elements. The meshes between the bundles contained granular layers of bioplasson, with a number of inflammatory elements, and also a moderate amount of capillary blood-vessels. In this layer, all stages of newly developing connective tissue could be observed; clusters of medullary or inflammatory elements; clusters in which these elements had already assumed an oblong or spindle shape; delicate spindles, closely packed together and transformed into basis-substance, with a relatively small number of bioplasson bodies left.

FIG. 173.—WALL OF AN ABSCESS OF THE BRAIN. TRANSVERSE SECTION.

F, layer of fibrous connective tissue, *V*, nests of medullary elements, apparently produced by the proliferation of the endothelia of former blood-vessels. *M*, myxomatous portion, in the meshes of which numerous medullary elements are imbedded, either in a delicate fibrous reticulum, or in a light, homogeneous basis-substance. Magnified 500 diameters.

Beneath the above described layer of fibrous connective tissue, the so-called membrana pyogena of the older writers, there followed a broad layer of connective tissue, exhibiting all the characteristics of the variety termed myxomatous. The connective-tissue bundles, while dense in the innermost layer, had become loose in the myxomatous portion, changing to a more or less vertical course, and inclosing large meshes of a homogeneous basis-substance. The coarser bundles formed strings, which by inosculating with each other produced a reticulum, built up almost exclusively by spindle-shaped elements, partly transformed into basis-substance.

Within the meshes of this reticulum is contained a very delicate fibrous connective tissue, with numerous, mainly spindle-shaped, bioplasson bodies; large fields of the meshes hold an almost homogeneous or very slightly granular basis-substance. (See Fig. 173.) A number of capillary blood-vessels of a considerable size, and partly filled with red blood-corpuscles, were also met with. The endothelia of these capillaries were very large, and found

to take up the carmine stain much more readily than endothelia under normal conditions. Around the wreath formed by these endothelia, in many instances, a light space was present, which space was enclosed by a collection of spindle-shaped bodies—the perivascular sheath. Outside of this myxomatous layer of connective tissue, in the wall of the abscess, is seen the white substance, bounding the layer of connective tissue in a very nearly straight line, and considerably altered in structure, as will presently be described. In addition to the above-described changes within the wall of the abscess, one of the most striking phenomena exhibited in some of my specimens is the retrograde movement of already newly formed capillary blood-vessels into their embryonal state—namely, the dissolution of their walls into medullary or embryonal or indifferent elements, resulting in the formation of solid connective-tissue bundles.

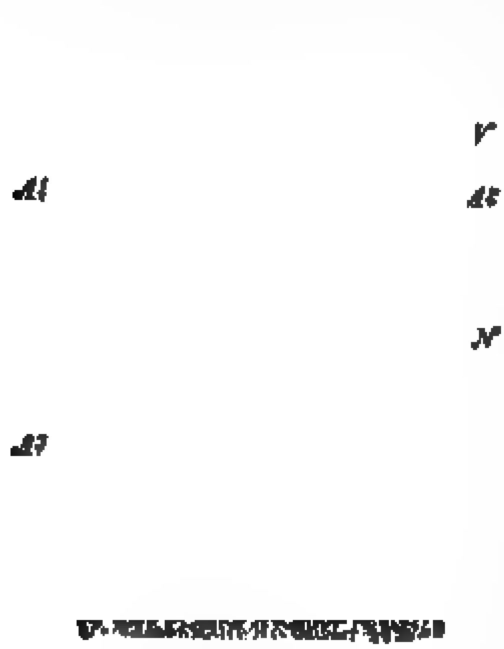


FIG. 174.—AXIS-CYLINDERS FROM THE BOUNDARY BETWEEN THE GRAY AND WHITE SUBSTANCE.

A^1, rosary-like, A^2, club-shaped, enlargement of the axis-cylinder, A^3, medullary elements arisen from the breaking apart of the axis-cylinder; N, nucleus of the gray substance in proliferation; V, vacuole. Magnified 1200 diameters.

(2) *White Substance.* The white substance around the abscess, as mentioned above, was in the condition of softening, and, even after careful preservation of the specimen, difficult to cut. With lower powers of the microscope, in the immediate vicinity of the abscess, the capillary blood-vessels of the white substance were seen to be considerably dilated and engorged with blood-corpuscles. The perivascular space, in many instances, was also dilated, and filled with a finely granular, evidently serous or albuminous, exudation. The changes in the nerve-tissue were best marked on the periphery of the blood-vessels. The nerve-fibers had lost their myeline-sheath to a considerable degree, and their axis-cylinders lay either bare or were surrounded by a layer of a faintly reticular bioplasson, which again was bounded by a thin homogeneous or granular sheath. Owing to a want of direct observation I am not enabled to tell what really had become of the myeline. It is, however, very probable that during the initial stages of the inflammatory process the myeline is dissolved out.

In many places the white substance was transformed into a finely granular mass, in which bioplasson bodies, so-called medullary elements, could be traced out, alternating with groups of shining homogeneous granules and of relatively little changed nerve-fibers.

Higher powers of the microscope gave a complete series of the changes of the axis-cylinders, which had led to the formation of medullary elements. (See Fig. 174.) First, the axis-cylinders exhibited delicate nodular enlargements and, at certain irregular intervals, a more regular rosary-like arrangement. In certain districts the axis-cylinder was transformed into a relatively coarse, shining, beaded fiber, also presenting a great many club-like enlargements. Next, some of the granules alongside the axis-cylinders appeared enlarged, and were provided with delicate vacuoles; and, lastly, the axis-

cylinders were transformed into a chain of pale bioplasson bodies, the so-called medullary or inflammatory elements.

Within the inflamed portion of the white substance were observed numerous varicosities, each of which was in direct connection with an axis-cylinder. In many instances, the interior of these varicosities could be made out to be of a delicate reticular structure; they were invariably bounded by a dense and homogeneous layer, continuous with the axis-cylinder. All the formations of the above description were uninterruptedly connected with each other by extremely delicate threads.

In some places small abscesses had formed outside the wall of the main abscess; these abscesses were detected only with the microscope. In such localities the medullary elements had assumed a more uniform size, a somewhat coarser granulation, and, having also lost their mutual connections, they were transformed into pus-corpuscles. As a matter of course, that portion of the white substance which had undergone such a change into pus-corpuscles was devoid of blood-vessels. The manner in which blood-vessels are lost, shortly before the tissues break down and are transformed into pus, was easily traceable in the neighborhood of such small abscesses. The endothelia of both the blood-vessel and the perivascular sheath became considerably enlarged, coarsely granular, or were supplied with at least several large shining granules, which might justifiably be considered as newly formed nuclei. By a process of splitting of the enlarged endothelia into medullary elements, the caliber of the blood-vessel, as well as of the perivascular sheath, became obstructed, and thus, what formerly had been a capillary, now was seen to have become transformed into a row of medullary elements. These at first remained in connection with each other by means of delicate processes, traversing the newly formed cement-substance, afterward broke apart and became pus-corpuscles, in shape and size fully identical with those sprung from other portions of the inflamed tissue.

The above-mentioned varicosities of the nerve-fibers, by different authors are considered as post-mortem changes, and due to an irregular coagulation of the myeline. The varicosities which I have described here have nothing to do with myeline, but are formations of the axis-cylinders themselves, and due to structural changes in the substance of these axis-cylinders proper—viz., enlargement of the thread, exhibiting the ordinary structure of bioplasson, and in close connection with the inflammatory changes of the nerve-fibers in general.

These changes in the axis-cylinders can be understood only if we look upon the latter as formations of living matter. In the inflammatory process, the granules of living matter in bioplasson bodies increase in size, sometimes to such an extent that the body is transformed into a shining, homogeneous lump, which readily divides into smaller particles, each of which in turn may become a medullary element. The axis-cylinders, being formations of living matter, also become coarsely granular, beaded, or rosary-like, and each one of these granular enlargements may give rise to a new medullary element, eventually a pus-corpuscle. In this manner we understand the formation of rows of medullary elements and of pus in the middle of the white substance of the brain.

Ever since J. Cohnheim asserted that the main, if not the only, source of inflammatory elements and pus-corpuscles are the emigrated colorless blood-corpuscles, some authors had entirely overlooked the changes taking place

in the constituent elements of an inflamed tissue. Nobody, nowadays, is intending to deny the emigration of colorless blood-corpuscles from capillary blood-vessels and small veins during the inflammatory process. Specimens obtained from the brain under consideration, by the immediate transportation of softened parts of the white and gray substance under the microscope, plainly demonstrated the existence of such a process. Along the wall of an enormously enlarged and engorged blood-vessel were seen colorless blood-corpuscles of a club shape, with one blunt extremity still in the caliber of the blood-vessel, with a thin pedicle still embedded in its wall, with the other blunt extremity protruding outside the periphery of the blood-vessel. Not infrequently a colorless blood-corpuscle was seen to be attached to the wall of the vessel by means of a slender pedicle, the main mass of the corpuscle being outside the wall of the blood-vessel or within the lumen of the perivascular space. There cannot be any doubt that the emigrated colorless blood-corpuscles share in the formation of pus-corpuscles, yet I lay stress upon the fact that the main source of inflammatory elements and pus-corpuscles must be looked for in the living substance of the inflamed tissue itself. More especially in the white substance of the brain under consideration, all the stages were traceable, from the granular enlargement of the living matter of an axis-cylinder up to the complete development and formation of inflammatory elements and pus-corpuscles therefrom.

(3) *Non-medullated Nerve-fibers.* A certain portion of my specimens, which was taken from the vicinity of the abscess, exhibited a large number of non-medullated nerve-fibers in bundles cut longitudinally and transversely. In the longitudinal bundles, the gray nerve-fibers were so closely packed together that but a very faint striation could be traced out. In the midst of such bundles there were numerous nests of medullary elements, of a prevailing oblong shape, and independent of any blood-vessels. Around these nests the following changes in the non-medullated nerve-fibers could be made out: First, the nerve-fibers had assumed a beaded or rosary-like appearance; next, they had become spindle-shaped and coarsely granular; after this, evidently from an increase in the size of the granules, the nerve-fibers had been transformed into an oblong cluster of bioplasson, within which, through the formation of a separating cement-substance, medullary elements made their appearance, in clusters, still retaining their spindle shapes. Lastly, a number of such spindle-shaped nests had coalesced, and rows and clusters of medullary elements could be seen, separated from each other only by a small number of unchanged non-medullated nerve-fibers.

Wherever such a transformation of nerve-fibers into clusters of medullary elements had taken place in a larger district, the result was the formation of an inflammatory nest, in which the elements were connected with each other by delicate threads. I have not seen an abscess in the middle of non-medullated nerve-fibers, but it is obvious from what I said before, that through the breaking apart of these medullary elements, as yet connected by delicate threads, pus-corpuscles may arise.

I claim, basing myself upon direct observation, that inflammatory foci, with crowded inflammatory elements, can arise from direct changes of the bare axis-cylinders constituting non-medullated nerve-fibers, independently of either blood-vessels or emigration of colorless blood-corpuscles.

(4) *Gray Substance.* In the vicinity of the abscess of the brain, I have met with a number of changes in the gray substance. First, the points of inter-

section of the living matter were enlarged, wherefrom resulted a coarse granulation of the gray substance. In many places, with the highest powers of the microscope, the points of intersection of the reticulum were clustered together to such an extent that lightly granular, nearly homogeneous, groups appeared, each of which was surrounded by a light rim. Owing to an augmented afflux of nourishing material, the formations of living matter had evidently very much increased in size, and by approaching each other produced densely granular or homogeneous lumps of living matter, with the appearance of indifferent or medullary elements. In certain places, the whole mass of the gray substance had been transformed into such medullary corpuscles, between which bundles of non-medullated nerve-fibers and blood-vessels, mainly capillary in nature, were still recognizable.

The nerve-fibers traversing the gray substance were mostly increased in size, and transformed into beaded fibers or chains of small homogeneous lumps. The blood-vessels, besides being completely obstructed with red blood-corpuscles, exhibited changes in their endothelial walls identical with those described above in connection with the white substance.

The nuclei of the gray substance were mostly very coarsely granular; the nucleoli especially had increased in size, and looked as if split up into a number of coarse granules. More especially in the carmine-stained specimens I often observed larger spaces, identical with the periganglionic space, either empty or holding extremely delicate granules. These spaces, so-called vacuoles, very probably had formed by an accumulation of a serous exudation around the nuclei, by which either a certain amount of the surrounding gray substance was pushed in a peripheral direction, or a certain amount of living matter destroyed. The fine granules within the above spaces, consequently, were either coagulated albumen or remnants of the former reticulum of living matter.

New formation of nuclei in the inflamed gray substance is of very common occurrence. Within the spaces just described I sometimes saw one large and two or three small nuclei, which, being in contact with their flattened surfaces, looking toward each other, allow of the conclusion that they had originated by a process of division of the original single nucleus.

New formation of nuclei, doubtless, takes place independently of former nuclei in the gray substance. I have seen repeatedly clusters of bioplasson near the wall of the abscess, with irregular outlines and holding a large number of oblong nuclei. Such multi-nuclear masses are evidently produced by the confluence of bioplasson bodies (emigrated colorless corpuscles—Ziegler), or by the formation of territories previous to their division into inflammatory elements.

The ganglionic elements within the inflamed brain-tissue exhibit a series of changes of great interest. Nearest to the abscess a number of ganglionic elements had swelled and been transformed into almost homogeneous, indistinctly granular bodies, still characterized by the presence of offshoots and a deep carmine stain. No doubt, the swelling of these elements is due to an inundation with exudation, which leads to a stretching and breaking apart of the reticulum of living matter therein.

The capillaries of regions where such swelled ganglionic elements are numerous are considerably dilated, their endothelial coat is partly thinned, partly thickened, by endogenous new growth, and their perivascular sheath enormously widened. In this space I have seen faint granules and pale gran-

ular bioplasson bodies of the size of colorless blood-corpuscles, indicating that immigration of such corpuscles had taken place.

In other portions of the gray substance a marked proliferation of the ganglionic bodies can be observed. There are bodies with enlarged and beaded nucleoli, bodies with two or three isolated nucleoli, bodies with two or three coarsely granular nuclei, sprung from a division of the original nucleus, as is proved by the presence of facets, where the nuclei lay against one another. (See Fig. 175.) Many ganglionic elements are transformed into coarsely granular, nearly homogeneous, lumps, and split into smaller lumps, varying in number from two to seven or eight. The clusters of bioplasson bodies are grouped together in such a way as to retain the general shape of the ganglionic body, considerably enlarged. The offshoots of these elements are in many instances still recognizable as being either enlarged and coarsely granular or broken apart into rows of bioplasson bodies.

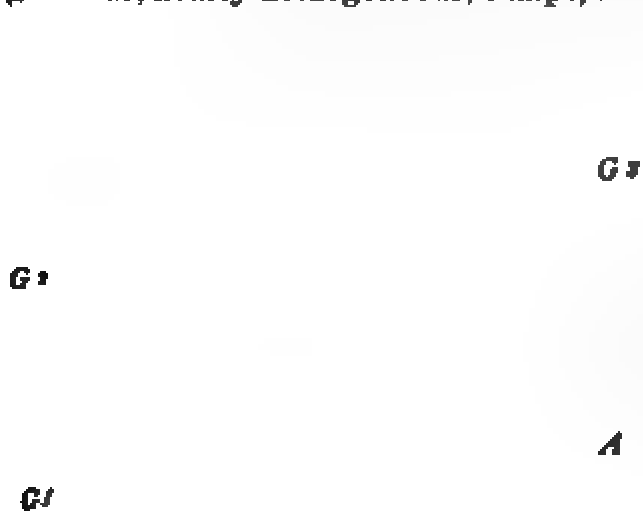


FIG. 175.—INFLAMMATORY CHANGES OF THE GANGLIONIC ELEMENTS OF THE GRAY SUBSTANCE OF THE BRAIN.

G^1, coarse granules and new nuclei in the body of the ganglionic element; G^2, splitting of the ganglionic element on its peripheral portion; G^3, the whole body transformed into medullary elements; A, axis-cylinder exhibiting the same change. Magnified 600 diameters.

As to the origin of medullary elements within the ganglionic bodies, I can state positively that they have originated by a process of endogenous growth from the bioplasson of the ganglionic bodies themselves. First, the living matter was increased, hence we explain the coarsely granular and homogeneous looks of such an element; next, marks of division had formed by the division of living matter into angular lumps, closely packed together so as to flatten each other, and separated by a thin layer of fluid, which everywhere was traversed by delicate conical offshoots, uninterruptedly connecting all newly formed lumps with each other. Some of these lumps, apparently, had further advanced in development than others; while some looked still shining and homogeneous, others were already coarsely granular, and presented a marked formation of a nucleus and a nucleolus. Again, all these formations, granules, nucleolus, and inclosing shells are united by delicate threads.

Lastly, the whole ganglionic element and its offshoots had broken apart into medullary or indifferent corpuscles, which, so long as they remain united to one another by delicate threads of living matter, represent an indifferent, medullary, or inflammatory tissue, identical with that arisen from the gray and white substance of the brain. If, on the contrary, the uniting offshoots be torn, the isolated medullary elements will produce pus-corpuscles, and an accumulation of such corpuscles gives rise to what is called an abscess. In the pus taken from the abscess of the brain under consideration, besides pus-corpuscles, a large number of bioplasson bodies were found suspended in the fluid, in size considerably exceeding that of ordinary pus-corpuscles.

These large bodies exhibited all stages of endogenous formations and proliferations of living matter, sufficiently indicating their origin from the ganglionic elements of the gray substance of the brain.

The *literature* on the subject of my studies is extremely sterile. No exact observations, at least to my knowledge, have as yet been made on acute encephalitis and suppuration of the brain substance. Only one point has so far been called attention to, and this is the proliferation of the ganglionic bodies of the gray substance. Th. Meynert * first noticed a proliferation of the nucleoli and nuclei of ganglion elements. E. Fleischl † found a division of ganglionic bodies, though not in a strictly inflammatory process, but in a brain involved in the formation of a tumor. A. R. Robinson ‡ produced inflammation in the ganglia of the sympathetic nerve around the aorta of the frog, and observed a division of the ganglionic elements from the formation of a furrow on the surface to the complete division into small particles. The division may involve only a part of a ganglionic body, the rest remaining normal, or it may invade the whole. Analogous transformations were also observed in the elongations of the ganglion cells.

Andrea Cecchirelli § produced traumatic lesions in the large hemispheres of the brain of a chicken and of rabbits. He saw enlarged and granular "ganglion cells" within the inflammatory focus, and came to the conclusion that the nuclei had increased in number and that the whole "ganglion cell," by division, had been transformed into smaller elements.

The results of my own observations can be summed up in the following points:

(1) The gray substance of the brain, by the inflammatory process, is transformed into inflammatory or medullary elements, in the production of which the nuclei and ganglionic bodies also share. Non-medullated nerve-fibers, through an increase of living matter in the axis-cylinders, are likewise transformed into medullary elements. The same results are produced in inflammation of the white substance of the brain, after the dissolution of the myeline.

(2) The medullary elements, sprung from the gray or the white substance of the brain, are transformed into connective tissue, either myxomatous or fibrous, and thus the wall of an abscess in the brain is the result of the reduction of the brain tissue first into medullary corpuscles, next into myxomatous, and lastly into fibrous connective tissue.

(3) Medullary elements, irrespective of which particular nerve-element they had originated, when broken apart, constitute pus-corpuscles, and, therefore, the contents of an abscess of the brain. In the fluid of the abscess clusters of bioplasson bodies are seen, proving a transformation of ganglionic elements into pus-corpuscles by a process of endogenous new formation and subsequent division of living matter. All the stages of this process are observable within the ganglionic bodies of the inflamed gray substance itself.

(4) The endothelia of the blood-vessels become enlarged, coarsely granular, and proliferating in the process of inflammation of the brain-tissue. New blood-vessels are formed in the wall of the abscess. A consolidation of the

* "Vierteljahrschrift für Psychiatrie," 1867.

† "Med. Jahrbücher," 1872.

‡ "Ueber die entzündlichen Veränderungen der Ganglionzellen des Sympathicus," Med. Jahrbücher, 1873.

§ "Ein Beitrag zur Kenntniss der entzündlichen Veränderungen des Gehirnes," Med. Jahrbücher, 1874.

blood-vessels, on the contrary, and a breaking up of their endothelia into medullary elements, afterward pus-corpuscles, takes place whenever the tissue is destroyed by suppuration. Pus is mainly a product of the inflamed tissue itself, and not of emigration of colorless blood-corpuscles.

4. Inflammation of Epithelia and Endothelia.

Epithelia and endothelia, being formations of living matter, respond in a very active manner to irritation. The changes of this tissue are not primary, as the inflammation invariably starts from the subjacent vascularized connective tissue. Even in mild cases of inflammation in connective tissue, the presence of an exudate can be demonstrated, which constitutes the condition known as "œdema." The surplus nourishing material is carried into the epithelia and endothelia from the blood-vessels, even though the irritating agent should be brought in direct contact with the epithelial or endothelial investment.

The inflammatory changes in this tissue, as in every other, consist in an increase of the living matter; the elements become what is termed "coarsely granular," or assume the "condition of cloudy swelling." If the inclosing shell of cement-substance is not immediately liquefied, a marked endogenous new formation of corpuscles takes place, resulting in the appearance of the so-called "mother cells"—*i. e.*, bioplasson bodies, containing a varying number of inflammatory elements, in all stages of development. We can trace the new formation of these elements from the coarse granules to the large homogeneous lumps, and, finally, to the nucleated plastids (see page 46). If, on the contrary, the cement-substance is liquefied in the early stages of inflammation, the living matter herein present—*i. e.*, the connecting filaments ("thorns")—is enlarged, and shares in the new formation in the same manner, as observed within the epithelial or endothelial elements. First, a number of these elements coalesce, and form large clusters of bioplasson, containing a varying number of nuclei and a large quantity of coarse granules, which, passing through the phases of bioplasson development, result in the production of inflammatory corpuscles. The final result of the inflammation is different, according to the *plastic or formative*, or the *suppurative nature* of the inflammatory process.

In plastic inflammation, the newly formed medullary or inflammatory corpuscles remain interconnected, and, becoming fusiform, give rise to *new formation of connective tissue*. The "cirr-

hotic" condition of the kidneys and the liver, f. i., is caused by the transformation of the epithelia into connective tissue, through the intermediate stage of medullary tissue. In suppurative inflammation, on the contrary, the connection of the medullary elements, which originated in the enlarged epithelia and endothelia, is broken, and the medullary plastids, now termed pus-corpuscles, are freed either by active emigration or by the contraction of the bioplasson of the parent body, which remains

FIG. 176.—BEGINNING OF THE PUSTULAR STAGE IN HÆMORRHAGIC SMALL-POX.

D, formation of homogeneous lumps from the bioplasson of the cuboidal epithelia; *E*, homogeneous and vacuoled lumps suspended in a finely granular, albuminous liquid. *C* (left), ledges of former cement-substance, the bioplasson of which has considerably increased in bulk; *C* (right), deepest layers of epithelia, compressed and rendered spindle-shaped, also with commencing increase of bioplasson. *O*, papillary layer, flattened and in the condition of oedematous swelling. Magnified 600 diameters.

comparatively little changed. The parent body itself, after the evacuation of the pus-corpuscles, presents a fenestrated appearance, with a varying number of vacuoles, indicating the location of the pus-corpuscles, or an apparently empty shell, pierced by delicate septa. All these formations are easily traced in the vesicular and pustular stages of small-pox. (See Fig. 176.)

Surface epithelia, if present in a single layer, are readily cast

off from the underlying membraneous connective tissue, and in the secretions are found to exhibit different degrees of an endogenous new formation of bioplasson. In the case of stratified epithelia, the outermost are shed off without marked changes, their bioplasson being lost in a horny metamorphosis. Sometimes the *nuclei* in these epithelia are seen to be homogeneous or coarsely granular, indicating that these formations are still endowed with a certain degree of vitality. The cuboidal epithelia of the middle, and the columnar epithelia of the deepest, layer show, in the most marked manner, the inflammatory changes described above.

Whether or not lost epithelia can be replaced by a new formation arising from the subjacent connective tissue is still an unsettled question, notwithstanding the numerous experiments which have been made. It is also unknown how the new formation of epithelia proceeds from former epithelia, although it probably takes place in the same manner, as will be described later on, in the article by L. Elsberg on papilloma—viz., from wedge-shaped bioplasson masses, springing from coalescence and growth of the inter-epithelial connecting filaments ("prickles"), imbedded in the cement-substance. That such a new formation is actually and rapidly going on is illustrated by the catarrhal inflammation of mucous membranes, in which great quantities of epithelia are lost, and again replaced after the inflammation has subsided. The cast-off epithelia of single layers are probably never completely restored.

A third series of changes of epithelia is observed in fibrinous or croupous inflammation. Here the epithelia are imbedded in, and saturated with, the exudate, and are either completely destroyed or only their nuclei are left. Such a destruction of epithelia takes place in the croupous inflammation of mucous membranes (Wagner) and in the croupous inflammation of the kidneys. The production of tubular casts in the latter disease is largely due to a degenerative metamorphosis of the epithelial elements of the uriniferous tubules.

Cornil and Ranvier were the first who maintained that in inflammation the endothelia are enlarged, and their nuclei divide and become the source from which pus-corpuscles are formed. The inflammatory changes of the *endothelia of the peritoneum (omentum)* have been studied most accurately by H. Kundrat. He noticed first a loss of the cement-substance, in place of which scattered globular bodies were seen. Next, enlargement and

division of the nucleoli and the nuclei of the endothelia followed. In recent peritonitis he found large multinuclear bodies, which greatly surpassed in size single endothelia, and in purulent peritonitis a marked new formation of inflammatory corpuscles, arising from the endothelia and leading to the formation of pus-corpuscles; but, probably, not all of these corpuscles are offspring of endothelia. Kundrat was the first to maintain that from the endothelia of the peritoneum, in chronic, plastic peritonitis, connective tissue arises, which leads to the formation of vegetations; and that this process takes place in two ways: either the endothelia themselves become spindle-shaped, elongated, and transformed into fibrillæ, or uniformly nucleated protoplasmic layers, sprung from the endothelia, become directly fibrillated.

The inflammatory changes of the *endothelia of blood-vessels* were studied by Virchow, Waldeyer, Ranvier, Thiersch, Durante, and others. Swelling of the endothelia, division of their nuclei, and new formation of inflammatory corpuscles from endothelia, have been proved to occur beyond any doubt. By some observers a direct transformation of endothelia into connective tissue is maintained. The occlusion of ligated vessels is mainly due to a proliferation of the innermost endothelia, and the vascularization of the thrombus is proved to start in the inflamed intima, and to proceed also from the adventitia and media. This is contrary to the views of C. O. Weber, who held that the coagulated blood of the thrombus itself becomes organized and vascularized. The coagulation of the blood was found to be caused by the inflammation of the endothelia.

In the foregoing article on encephalitis, by Beyer, repeated allusion is made to the inflammatory changes, both progressive and regressive, that take place in the endothelia of capillaries. From what I have observed, I can confidently state that the endothelia of the capillaries participate in the inflammatory process in a very active manner. In the earliest stages of inflammation the endothelia become at first enlarged and coarsely granular, in consequence of which the caliber of the vessel is considerably narrowed. Next, the endothelia enter the juvenile stage of bioplasson by becoming homogeneous, and through their confluence render the formerly hollow bioplasson a solid, homogeneous cord, in which afterward a differentiation into medullary or inflammatory corpuscles takes place. Such corpuscles may sometimes spring directly from the capillary endothelia, without previous solidification of the blood-vessel. *The result is, that in acute inflam-*

mation a large number of capillary blood-vessels are destroyed—i. e., transformed into the inflammatory new formation. Should the inflammatory corpuscles separate and produce pus, a permanent destruction of the vessels ensues. If, on the contrary, the inflammation should not pass the stage of tissue-formation,—*i. e.*, become plastic and formative,—an active new formation of blood-vessels in the middle of the inflamed tissue will follow, independently of the former and older blood-vessels, and to an extent far exceeding the former vascularity. Most of these newly formed blood-vessels contain newly formed red blood-corpuscles. The manner of new formation of blood and blood-vessels is dwelt upon on page 373. Should new formation of blood-vessels in an inflamed tissue not take place, the tissue will represent what is termed a "tubercle," and undergo different secondary changes.

The endogenous new formation of elements within the epithelia was first maintained by Remak in physiological, and afterward by Buhl, Rindfleisch, and others in pathological, conditions, and its existence thoroughly proved by L. Oser. In opposition to the view that the corpuscles visible in the endothelia had immigrated from without, Oser demonstrated the origin of inflammatory corpuscles *within* the epithelia. My own researches fully corroborate the statements of Oser.

Varieties of Inflammation.

From my statements it follows that I consider the presence of blood-vessels to be a requisite for the production of an inflammatory process. As only connective tissue is supplied with blood-vessels, it necessarily follows that the primary seat of inflammation must always be in the connective tissue, and that the structural changes of muscles, nerves, and epithelia are secondary to, though, perhaps, almost simultaneous with, those of the connective tissue. An independent inflammation of epithelia never occurs. I, therefore, consider the terms of "interstitial," "parenchymatous," etc., inflammation as superfluous, except for clinical purposes.

Emigration of colorless blood-corpuscles unquestionably occurs, even in the earliest stages of inflammation, probably preceding structural tissue changes. Such an emigration may also participate in the formation of pus-corpuscles, so long as the blood-vessels are not destroyed. The principal change, however,

more particularly concerns the invaded tissues themselves. They are first reduced to their juvenile condition; their medullary elements, by endogenous or exogenous new formation or simple division, give rise to a new formation of inflammatory corpuscles. If these remain interconnected, a new formation of tissues, in most instances, and most predominantly of connective tissue, takes place; thus, "hypertrophy" or "hyperplasia" is established. If, on the contrary, the inflammatory corpuscles become separated, pus-corpuscles arise from the inflamed tissue, either forming an abscess or leading to pyorrhœa or empyema. The question, how many of the pus-corpuscles owe their origin to emigration of colorless blood-corpuscles, cannot be answered positively.

Considering both the nature of the exudation and the tissue changes, there is no good reason to abandon the old terminology of "humoral pathology" for the designation of different forms of inflammation—such as catarrhal, croupous, etc. These, it is true, differ only in degree, but the names, having been once adopted, may be used, as heretofore.

(a) Catarrhal inflammation consists of a serous exudation, a partial reduction of the connective tissue into its juvenile condition, an increased secretion, proliferation, and shedding of the epithelia. In acute *catarrhal inflammation* the predominant features are the serous exudation, the augmented secretion, and shedding of the epithelia from the free surfaces and in glandular organs; there is, in addition, a hyperæmia of the subjacent connective tissue. In *subacute or chronic catarrhal inflammation* the augmented secretion and shedding of the epithelia persists, and the subjacent connective tissue is hypertrophied, with a more or less new formation of blood-vessels, or, on the contrary, reduced in bulk—atrophy. In closed or occluded glandular cavities the epithelia are transformed into medullary corpuscles, from which new connective tissue arises—cirrhosis.

(b) Croupous inflammation consists of a fibrinous exudation and a partial reduction of the connective tissue into its juvenile condition, while the epithelia, by their imbibition of the fibrinous exudate, are destroyed. In *acute croupous inflammation* the exudate is sometimes fibrinous, sometimes modified albuminous. On free mucous surfaces and in glandular organs the epithelia are destroyed; these, with intense hyperæmia, hæmorrhage, and inflammation of the connective tissue, are the main symptoms. In *subacute or chronic croupous inflammation* the exudation is

modified, often containing the so-called colloid or waxy material. The subjacent tissue is hypertrophied, and, in certain districts, the epithelia are completely destroyed and a profuse new formation of fibrous connective tissue is produced. This condition is called atrophy.

Diphtheritic inflammation consists of a fibrinous exudate in the substance of the connective tissue, with an isolation of portions of this tissue, and their subsequent death—viz.: putrefaction and throwing off of the so-called membrane. Organisms of decomposition, micrococci and bacteria, are secondary products of putrefaction. For a long time the difference between croupous and diphtheritic inflammation was held to be that in the former the exudate forms on the surface, in the latter in the substance of the tissue itself; but they are, in essential points, identical processes.

(c) Suppurative inflammation consists of an albuminous exudation, a complete breaking down of the connective, muscle-, or nerve-tissues, and of all blood-vessels, into pus-corpuscles, also a new formation of these corpuscles from epithelia. *Acute suppurative inflammation* results in the formation of an abscess in the middle of the tissue, or a flow of pus from free surfaces,—the so-called pyorrhœa, or an accumulation of pus in closed cavities—the so-called empyema. Blennorrhœa and intense catarrhal inflammation blend with suppuration, and may be either acute or chronic. *Chronic suppurative inflammation* is characterized by intense hyperplasia of the connective tissue, together with persistent augmented secretion and a partial destruction of blood-vessels and tissues—the *ulceration.*

The healing process of wounds by suppuration is accompanied by an active outgrowth of freely vascularized, newly formed, connective tissue, which is at first of the myxomatous variety, and is termed granulation tissue. How much pus is produced by emigration of colorless blood-corpuscles in blennorrhœa, pyorrhœa, and in healing and granulating wounds, we are unable to say. The originally myxomatous tissue of granulating wounds is changed into fibrous connective tissue; the at first numerous blood-vessels are, to a great extent, also transformed into fibrous tissue, and these processes terminate finally in a *scar, cicatrix.*

If the inflammatory new formation be not supplied with newly formed blood-vessels it is called a tubercle, and the totality of the avascular new formation represents the tuberculous mass, which, by the breaking and the shrinkage of the inflammatory corpuscles, becomes "cheesy." Tubercle, therefore, with some reason, may be termed a dry abscess.

No allusion is made in this chapter to the parasitic origin of the inflammatory process, especially the germ theory, as applied to inflammation. Unquestionably, organisms of decomposition, if brought into the interior of a living tissue, or, perhaps, even only in contact with it, will excite inflamma-

tion or necrosis. But how much is true of the "specificity" of such low organisms, as regards malarial fever, recurrent fever, typhoid fever, syphilis, leprosy, diphtheria, etc., is a question which to-day cannot be positively answered, as the sources of mistake, both in experimental and microscopical research, are too many and too little under our control. What the infecting germs of measles, scarlet-fever, and small-pox are, we do not know.

Secondary Changes. Among the disturbances of nutrition, partly considered as inflammatory, partly unknown in their origin, three deserve mentioning—namely, the fatty, the pigmentary, and the waxy degeneration.

Fatty Degeneration. As mentioned before (see page 155), the fat-granules are directly produced from granules of bioplasson. Every living tissue, in a physiological or pathological process, may exhibit fat-granules, both in its free bioplasson bodies and in the interstitial substances. In this latter situation, also, the fat originates from the bioplasson formations. In the myxomatous and fibrous variety of connective tissue the fat is a normal product, at least to a certain degree; cartilage corpuscles often exhibit fat granules and globules, even in middle-aged individuals. In chronic inflammation of cartilage and bone, especially in their ulcerative destruction, in caries, fat-granules are very common occurrences in the plastids. In muscles, fat-granules arise from a direct transformation of the sarcous elements: in paralyzed and atrophied muscles, from want of exercise; in typhoid fever; in the muscle of the heart, either as an independent pathological process, or in connection with hypertrophy. In higher degrees of fatty degeneration of the muscle of the heart, nearly the whole organ, but principally the left ventricular wall assumes a yellow color, and the tissue becomes quite brittle. Most of the sarcous elements have been converted into fat-granules, which slightly exceed the original sarcous elements in size; they still remain interconnected, however, by delicate filaments. In the ganglionic elements of nerve-tissue, fat-granules are often met with; this always indicates a disturbance in the intellectual, sensitive, or motor centers. I have seen fatty degeneration of the axis-cylinders of nerves, resected for the relief of neuralgia, caused by the so-called perineuritis—*i. e.*, chronic inflammation of the external and internal perineurium. In epithelia and endothelia fatty degeneration also occurs, reaching its highest degree in the epithelia of the liver. Wedl has demonstrated fatty degeneration even in the cement-substance of epithelia perfectly healthy. A rare and sometimes intra-

uterine process is the fatty and pigmentary degeneration of the covering endothelia of the heart, probably caused by pericarditis. (See Fig. 177.)

Tissues in fatty degeneration are often subject to calcareous depositions, both processes being indicative of a lowered nutrition of the bioplasson, the causes of which are not clearly understood.

Pigmentary degeneration is closely allied to fatty degeneration. Even under normal conditions fat-globules may contain a diffuse or granular coloring matter, and fatty and pigment degenerations are often found combined. We have no chemical analysis of the pigment; but its source is unquestionably the coloring matter of the blood. Extravasated blood, after a while, produces rhomboidal or needle-shaped crystals of hæmatoidine, which are in color dark reddish-brown. (See chapter on urine.) If the coloring matter be imbibed by living plastids, pigment-granules of a rust-brown or brownish black color will be seen in these bodies. The rusty color of the tissue, sometimes seen abounding in old, healed apoplectic focus in the brain, is due to the presence of pigment-granules. Rokitansky maintained, in 1846, that in melanotic cancer the pigment is supplied by the blood, which originates in the mother cells. My own researches, made especially in the boundaries of melanotic myeloma of the choroid invading the vitreous body, demonstrate that the sources of the pigment are the hæmatoblasts—i. e., lumps of living matter, saturated with coloring matter (hæmoglobin?) of the blood. The points of intersection of the bioplasson reticulum within these plastids are enlarged, and assume a dark yellow or brown tint, remaining, however, in connection with the reticulum. By coalescence of the granules pig-

FIG. 177.—FATTY AND PIGMENTARY DEGENERATION OF THE PERICARDIAL ENDOTHELIUM OF THE HEART OF A CHILD.

F, endothelia, exhibiting the beginning of fatty change of the granules of bioplasson, *P*, endothelia, with pigment granules in their interior. Magnified 600 diameters.

lusters originate, which may still remain connected with changed bioplasson; and if the granules are present in large rs they may conceal the nucleus of the plastid, which, as a oth in physiological and pathological pigment formations, is unchanged. (See Fig. 177.) All varieties of tissues may e the seat of pigmentary degeneration, and it is evident, par-ly in melanotic cancer, that both the connective tissue and wly formed epithelial plastids are more or less abundantly ed with granules and clusters of coloring matter. Rust- pigmentation is sometimes observed in the sarcous elements ated muscles, in the gray substance, and the ganglionic cor-s of the nerve-centers, independently of former hæmorrhage. act that it is the living matter itself which is transformed igment, facilitates the understanding of the very rapid earance of pigment—f. i., from the epithelia of the skin e medullary tissue of the hair-bulb.

xy degeneration. In chronic ailments, such as syphilis, pro-appuration, caries of bone, etc., and in the placenta even in ntly healthy women, a peculiar change of the tissues, called takes place, which leads to an increase of bulk, a paling of olor, due to compression and obliteration of blood-vessels, n increase of weight and consistence. There is a general ance of the tissue similar to that of wax or lard; hence the ' lardaceous," which is also used to designate this change. stionably, this degeneration is due to a chemical change of asma of blood, as it is sometimes found in hæmorrhagic independent of, or combined with, analogous tissue changes. this change really consists in we do not know, and it is a hypothesis of Dickinson's to call the waxy substance "de-zed fibrine."

e appearance of waxy degeneration varies in different s and organs. The chemical reactions are not always ame; neither are the stainings with carmine and ani-olors always productive of the same results. The myxom-variety of connective tissue is not infrequently the seat xy degeneration. (See article on waxy degeneration of lacenta.) In certain diseases the medullary tissue of is invaded by this change, which leads to the formation bules termed "colloid corpuscles," which are remarkably ponsive to the usually destructive action of acids and alka-(See article on osteomalacia.) In the myxomatous tissue thymus body such homogeneous or concentrically striated

corpuscles are, as a rule, found after the involution of the organ. Among the blood-vessels, the arteries of the spleen are often seen in waxy degeneration before the other constituent parts are attacked. (See Fig. 178.) The degeneration starts in the smooth muscle-fibers of the middle coat; these are enlarged, transformed into a homogeneous mass, in which no trace of structure or of nuclei can be recognized. In the kidneys, the waxy change is sometimes observed in the walls of the capillaries sooner than in the arteries. In the liver, waxy degeneration takes place independently of the blood-vessels.

Muscle-tissue is often subject to this degeneration, especially

FIG. 178.—WAXY DEGENERATION OF AN ARTERY OF THE SPLEEN OF A MAN AFFECTED WITH SYPHILIS.

E, endothelial coat of artery, *M*, muscle-coat of artery, in waxy degeneration; *B*, bundles of smooth muscle-fibers accompanying the artery; *D*, lymph-corpuscles in the myxomatous reticulum. Magnified 600 diameters.

the muscle of the heart, predominantly the wall of the left ventricle, by which this structure is enlarged, rendered friable, and of a peculiar lardaceous luster.

Waxy degeneration is often found in nerve-tissue, both in the gray substance and the ganglionic elements, in connection with similar changes in the walls of the blood-vessels, and also without

h changes. For particulars I refer to the two following . Epithelia and endothelia are likewise subject to this ration—f. i., in the liver, the kidneys. The epithelia of the ometimes give rise to homogeneous or concentrically stri-lloid corpuscles, and such are sometimes observed in the a of the prostate gland. The concentric colloid corpus-the latter organ may become the seat of calcareous depo-and are sometimes voided with the urine. They are not mmon occurrence. (See chapter on urine.)

uliar, but certainly kindred, formations are the *colloid les of the nervous system.* Usually they exhibit a concentric n; sometimes two or more such concentrically striated cles may be surrounded by a common homogeneous or l layer. (See Fig. 179.) Virchow, by mistake, termed

79.—Colloid or Amylaceous Corpuscles of the Arachnoid of the Spinal Cord of an Adult.

entrically striated amyloid corpuscle; *G*, group of medullary corpuscles in colloid on; *L*, medullary corpuscles in the beginning of colloid degeneration. Magnified ers.

amylaceous" corpuscles. In the arachnoid of a man rain, crowded with these corpuscles, was in the condition o-called "gray atrophy," I could trace the origin of these ons from medullary elements, which had arisen in the tissue of the arachnoid in consequence, evidently, of a

slight inflammatory process. The medullary corpuscles, being infiltrated with the colloid material, either remained in irregular groups, or, becoming elongated, gave rise to the concentrically striated corpuscles, in a way similar to that in which the territories of connective tissue are formed. In the center, sometimes an unchanged plastid is seen, or a larger homogeneous mass, or a shallow depression, termed an umbilicus.

Waxy Degeneration of the Cerebellum. By J. Baxter Emerson.*

Mr. B. was the youngest of a family of seven children. His mother died of acute encephalitis, terminating in abscess; a maternal uncle and aunt both showed symptoms of dementia late in life. One of his sisters has suffered for several years with hysteria; a second sister has at the present time posterior spinal sclerosis. When about fifteen years old, he was thrown from a carriage, and received a severe scalp wound on the posterior part of his head, from which he seemed to recover. His habits were regular. He was much troubled with naso-pharyngeal catarrh. At the age of twenty-eight he lost all his property, which worried him excessively; soon he found that he was losing flesh and strength, that his appetite was poor and his digestion bad; his also had the tendency to fall when walking or on turning suddenly. He brother noticed that he became slower in his work. In January, 1874, the above symptoms returned; he began to stammer, and would often forget localities and names. These symptoms were intermittent in character; at times he was apparently well. In September, 1874, he was married, and while on his wedding trip, his wife noticed that if he endeavored to walk down a flight of steps, he would become pale and complain of vertigo. Shortly afterward he was attacked with most intense pain in the head, accompanied with great irritability, photophobia, and inability to stand alone. These acute symptoms lasted several days, and for several weeks he had to be led to prevent his falling. About a month later he had a second similar attack, this time losing the power of speech and being "delirious." Later, he complained of "pain in the forehead," numbness of the extremities, occasional twitching of the muscles, and he was unable to walk without assistance. On two occasions he asserted that he was blind, which assertion he persisted in for two days. He was exceedingly childish in his actions. Toward the latter part of the summer of 1876, he became violent, his hallucinations and delusions being of an exalted character.

On October 5, 1876, I found his left pupil dilated, the tongue tremulous, the power of coördinating the muscles much impaired, those of the left side more so than the right; the left biceps permanently contracted, so as to keep the fore-arm at an angle of about one hundred and thirty-five degrees with the axis of the arm; contractile power of the muscles on the right side more marked than on the left; an almost incessant movement of either the fore-arm and hand, or grinding of the teeth; partial anæsthesia of the left side; aphasia of both varieties, but principally amnesic; hallucinations and delusions of a very exalted character, seeming to dwell principally on financial

* Abstract of the paper "Peri-encephalitis," by J. Baxter Emerson, M. D., New-York. *Journal of Nervous and Mental Disease.* Chicago, April, 1880.

subjects; emotions not under control; sense of decency lost; using the most obscene language; responding to calls of nature regardless of surrounding circumstances; dementia very marked, at times so violent as to necessitate restraint; insomnia.

On November 14, 1876, he had an attack, with the following symptoms: Complete left hemiplegia and hemianæsthesia; complete aphasia; congestion of head and neck; extremities cold, especially the left; head drawn to the right, and fixed; both eyeballs drawn to the right; left pupil widely dilated; conscious, with sense of sight and hearing intact; facial muscles slightly paralyzed on the right side; those of deglutition interfered with; respiration irregular and sighing in character; pulse 84, irregular and intermittent; temperature 100°. Soon after, the muscles of the paralyzed side began to twitch, first in the extremities, gradually extending to the trunk, until, finally, all the muscles of the left side were in a constant state of spasmodic contraction. The next morning the symptoms were all gone, except slight paralysis and aphasia, and the patient apparently better than before the attack. These attacks, of varying intensity, occurred about once a month during the remainder of the patient's life. Dementia became more marked. He persisted in keeping up the movements of his right fore-arm and the grinding of his teeth to the last; consequently, their muscles retained the normal size, while all others underwent atrophy from disuse; but to the day of his death he was able to walk with assistance. His urine was normal to the last, but he had retention for five days previous to his death, which occurred May 13, 1879, from exhaustion.

A post-mortem examination gave the following results: Body much emaciated; ulcer, the size of a dime, on sacrum. Dura mater much thickened throughout its whole extent, adherent to the pia mater in spots, and firmly adherent along sup. long. sinus and in the temporal regions, much more so on the left side than on the right. The pia mater was much thickened and congested, and had numerous hæmorrhages, from the size of a pin's head to that of a split pea, imbedded in its structure. These were principally on the left side, all confined to the upper surface. The pia mater was adherent to the base of the skull and the brain, in spots. The brain was much congested, weight 40 oz. The convolutions on the right side seemed deeper, and the gray matter thicker than on the left. The white substance was slightly darker than normal, and much congested. The consistency of the whole normal, and all other parts negative.

A large portion of both hemispheres was removed and placed in Müller's fluid, then in a weak solution of chromic acid, until it was sufficiently hard for section, after which it was kept in dilute alcohol.

The pia mater was composed principally of bundles of decussating fibers of connective tissue, coarser than normal, traversed by dilated and enlarged blood-vessels, distended with blood, and around many of them were bundles of spindles and inflammatory elements. This condition of connective tissue is characteristic of an inflammatory process of chronic nature, which process led to the formation of new connective tissue, while an acute recurrence of the same process has given rise to a new formation of inflammatory elements. The dura mater was found structurally in the same condition as the pia mater, but had no hæmorrhages in it.

A vertical section through either hemisphere of the cerebellum with a low power of the microscope gave the following appearance: The blood-vessels

could be traced from the pia mater, especially in the sulci between the convolutions, through the external gray and granular layers into the white substance, profusely branching and ramifying, and almost invariably engorged with blood. In numerous places there were ramifications closely resembling those of the capillaries, with sharp, well-defined, fluting outlines, colorless, and of a high refractive power. Such groups were found principally in the granular layer, but extended somewhat into the contiguous layers. There were also numerous isolated, highly refracting bodies, scattered throughout the whole cerebellum, but mainly in the granular layer. With a higher power of the microscope, peculiar changes of the capillaries were shown, first described by C. Wedl—namely, the capillaries were transformed into either single or double rows of brilliant, colorless globules, or completely transformed into a glistening rod-like mass, with fluting outlines, and numerous, partly pedunculated, buds. The large isolated bodies had all the characteristics of the corpora amylacea—namely, they were concentrically striated and umbilicated. In some instances, the umbilicus was found in direct union with capillaries, which had undergone the above described changes. Exceptionally, I found the "cells of Purkinje," with their offshoots, presenting the same glistening, highly refractive, appearance as the capillaries and corpora amylacea. Some of the latter looked as if they were composed of a number of shining globules, closely packed together, the outlines of the globules being just traceable within the clusters.

I used the following re-agents: *Carmine* (both ammonia and alum solutions), which stained the tissues, but left the globules colorless. *Iodine* (both tincture and aqueous solution, both with and without sulphuric acid); the result was unsatisfactory, for only once, after the use of the aqueous solution, did I perceive any change in the globular bodies, and then the pale blue tint was very indistinct, and only a few of the bodies affected. *Hæmatoxylon* produced a distinct violet upon the tissues and the blood-vessels, while the globules were little affected, if any, by it. *Chloride of gold* (one-half per cent solution) made the outlines more distinct, but did not change the color of the globules. *Violet methylaniline* stained the granular layer a deep blue, the external gray layers and the white substance a dirty grayish-blue; the blood-vessels both in the normal and pathological condition were unaffected. *Fuchsine* produced a pink stain in the gray layers; the globular bodies and blood-vessels were untouched. *Osmic acid* (one per cent. solution) produced a marked brown discoloration on the globules, but by no means as deep as that we are accustomed to see on fat-globules. *Picro-indigo* gave the blood-vessels and globules a bright green color, while the surrounding tissues were of a much paler tint of green.

In unstained specimens, the refractive power of the globules and corpora amylacea was so characteristic as to allow of no diagnosis, except calcareous degeneration of capillaries, of corpora amylacea, and exceptionally of "cells of Purkinje." In the whole list of my re-agents there was nothing found contradictory to this, though, I must admit, very little to confirm it. The capillary blood-vessels in several instances showed rows of calcareous globules on both walls, while in the center a row of blood-corpuscles was still recognizable in that portion of the capillary nearest the pia mater, while the central end of the capillary was completely filled with the shining globules. The change, therefore, which led to the formation of these globules must have taken place in the walls of the capillaries, and in turn has led to the consolidation of the entire blood-vessel.

highest powers of the microscope (1200 diameters) showed in many ries of the cerebellum an enlargement of the endothelia, with a coarser ization therein, and a splitting of the original endothelia into coarsely ar clusters. The perivascular sheaths in some instances were considerilated and sometimes filled with globular elements, slightly increased ractive power. From the above facts it would seem that the shining ar bodies are products of the endothelia, which first become inflamed, roliferate, and the inflammatory elements thus formed become infilwith lime-salts. Concerning the formation of the corpora amylacea, present know nothing. The gray layers of the cerebellum with a high of the microscope showed a reticular structure. The white substance cerebellum was composed almost exclusively of nerve-fibers with ous varicosities, and a reticular structure was seen in the nerve-fiber l as in the varicosities. On broken ends of nerves, I could trace several -like layers, composed of a row of spindles, bounding the swollen pearl ends of the nerve-fiber, while the center of the so formed body showed ate reticular structure. Such formations, we know, never are seen so myeline is present. It therefore follows that either the myeline has out after death, or has been absorbed during life, perhaps in the same r that adipose tissue disappears in wasting diseases. The boundary f the nerve-fiber in all instances was shining and homogeneous, thus nting a complete sheath. There is no reason, therefore, to my mind, ying the existence of a sheath in the nerves of the white substance of ebellum, and I may also add cerebrum, for they were both similar in se.

gray substance of the cerebrum was similar in structure to that of the lum. The calcareous corpora amylacea were less frequently, and the ous globules exceptionally, found. The blood-vessels were, as a rule, ed with blood. The perivascular sheaths were, in some instances, . Several specimens showed a fatty degeneration of the blood-vessels the ganglionic bodies, both demonstrated by their refraction and by ion on them of osmic acid, which produced a black stain. The fats were arranged in the ganglionic bodies in a crescent shape, the conbeing on one side of the ganglion, and the concavity toward the . In the cerebrum I frequently found empty spaces, as they were lso in the cerebellum—so-called vacuoles.* Most of the vacuoles had : interior a pale nucleus, and their origin must be attributed to an lation of fluid around the nucleus after death, or to a hydropic destructhe ganglionic elements, due to serous exudation. The latter view is rated by similar formations around the blood-vessels, where not only heaths were found dilated, containing bioplasson elements, but there a large space around the lymph-sheath. Several ganglionic bodies rtly fatty degeneration also showed closed empty spaces on the ry.

diagnosis, as obtained from the microscope, in this case is *chronic eningitis, meningitis, and encephalitis, terminating in atrophy.*

r observations in the gray substance of the brain and the spinal cord, which aded by atrophy, due to chronic encephalitis and myelitis, demonstrated that the n reticulum was more or less rarified—viz.: its meshes enlarged. There is a gradual of enlarged mesh-spaces to still larger spaces, termed vacuoles. I am unable to say omes of the bioplasson in such a wasting process.—ED.

WAXY DEGENERATION OF THE BRAIN. BY JOHN A. ROCKWELL, M. D.*

The pathology of the central nervous system has as yet been very little elucidated, for the simple reason that its minute anatomy has not as yet been fully understood.

The reticulum in the gray substance, first described by J. Gerlach, and by L. Mauthner, twenty years ago, has been considered to be nervous in nature, as both observers saw this reticulum in direct communication with axis-cylinders. Quite recently, however, this assertion has been contradicted by S. Stricker and L. Unger, who claim that the reticulum is an elongation of the pia mater, and therefore of connective-tissue nature. So far as my experience goes, I must coincide with the views held by Gerlach and Mauthner. I invariably succeeded in staining the reticulum of the gray substance violet with a solution of chloride of gold, the same as the nuclei which are scattered throughout the gray matter, and the ganglionic elements, whose nervous nature cannot be questioned. Moreover, I saw the reticulum in connection with axis-cylinders, which we also know to be positively nervous elements.

It seems to me that the question, What is connective tissue, and what is nervous structure in the gray substance? will never be definitely answered, as the connective-tissue offshoots of the pia mater, upon reaching the finest ramifications, lose their basis-substance and become bioplasson in nature, the same as the nervous structure itself. C. Wedl was the first to maintain that a waxy degeneration may invade the capillary blood-vessels, resulting in the formation of shining, homogeneous cords, ramifying like blood-vessels and freely supplied with pedunculated, bud-like, stratified projections.

The amylaceous corpuscles have, for a long time, been known to occur in the gray substance of the central nervous system, where they represent bright, stratified, apparently structureless masses, containing sometimes in their central portion an unaltered plastid. Such corpuscles are so common, both in the gray substance of the brain and the spinal cord, and in the arachnoid of each, that some histologists have asserted that they were normal formations. They occur either singly or in double or multiple formations, clustered and partly coalesced. Their designation, "amylaceous," originated with Virchow, who, upon applying iodine and dilute sulphuric acid, could in some instances produce a bluish tinge of these corpuscles. Upon the authority of Virchow the name "amylaceous corpuscles" has been accepted, although the bluish color after treatment with iodine — which feature reminded Virchow of starch corpuscles of plants — by later observers could not, or only in a very slight degree, be produced. Evidently, the bluish color, wherever it occurs, is nothing but the complementary color of these highly refracting bodies to the yellow-brown neighborhood after the application of iodine. I consider this re-agent of no value.

What the intimate nature of the amylaceous corpuscles, or the waxy degeneration in general, is, we do not know. This much is certain, that the formation of these corpuscles, as well as the waxy degeneration itself, is closely connected with chemical alteration of the plasma of the blood, inasmuch as in almost all instances the waxy change is known to first invade the blood-vessels. In the spleen and the kidneys the muscle-coat of the small

* Abstract of the paper, by John A. Rockwell, "A Contribution to the Pathology of the Brain." *The New England Medical Gazette*, March, 1882.

arterioles is, as a rule, the first to exhibit the waxy change. In the brain, the capillaries are unquestionably the first invaded formations, as recently proved again by J. Baxter Emerson. The case from which my specimen has come was one for two years under the observatien of Dr. E. H. Linnell, of Norwich, Conn.*

"Mr. T——, aged sixty-three, of nervous temperament and thin habit, first consulted me," says Dr. Linnell, "for failing vision, in November, 1879. His vocation had been that of a photographer, until ill health obliged him to relinquish it. Inquiry elicited the following facts: For the past eight or nine years he had been subject to frequent attacks of neuralgia, affecting his head and limbs; he had been habitually constipated; his urine had been somewhat increased in quantity, light-colored, and passed frequently; and for four years he had had paralysis agitans, affecting his right arm and leg, but more markedly the arm. This tremor developed gradually, and was attended with partial anæsthesia, denoted by numbness and tingling sensations in the affected limbs, and by general debility. In other respects he enjoyed good health until the fall of 1879. During the night of September 27th, of that year, he had a sudden severe attack of pain in the head, extending from vertex to chin, accompanied by total blindness, and followed by vertigo, nausea, and slow pulse. After twenty-four hours the intensity of symptoms was moderated, and his sight began very gradually to be restored, but was never fully recovered. He continued to suffer with neuralgic headache and vertigo, and his gait became halting and uncertain. His mental faculties, however, remained unimpaired, and the paralysis agitans, or the difficulty of locomotion, did not increase. When I first saw him, VOU = $\frac{20}{50}$, refraction Em. He had, however, left-sided binocular hemianopsia. . . . In the latter part of April, 1880, he had another sudden attack of complete blindness. This attack was unattended by pain, and was of shorter duration than the first. During the following year his sight seemed to fail gradually, until he could with difficulty distinguish large objects. He complained much of dizziness, but suffered less pain; walking became more fatiguing, the right leg seeming heavy, and as if too long. He retained the use of all his faculties, and could converse intelligently, although his mind seemed to lose some of its natural vigor. In the latter part of June, 1881, he was suddenly seized with a general tremor of the whole body, afterwards becoming more pronounced upon the right side. This was not attended with pain, and he apparently recovered from the effects of it; but had a similar seizure July 2, accompanied with constriction of the post-cervical muscles. The rigidity increased, he soon became unconscious, and was apparently entirely blind. After a few hours he partly regained consciousness, and had perception of light. From July 4 to 8, he seemed to improve somewhat. From this time he gradually failed, both in intellect and strength, until he became comatose, in which condition he remained for several days, and died July 19.

"Autopsy gave the following result: The dura mater was so firmly adherent that the calvarium could not be removed without cutting; and in so doing, several ounces of dark fluid blood escaped from the sinuses. Both the dura mater and the arachnoid appeared healthy. The pia mater was much injected, the veins being distended with dark blood. The entire weight of the brain was two pounds, fifteen and one-half ounces. The cortical substance of the cerebrum was of normal consistence; but upon section of the right hemi-

* Published in the "Archives of Ophthalmology," vol. x., No. 4, December, 1881.

sphere, a large and firm coagulum was found in the medullary substance. It was nearly circular, and measured, approximately, four centimeters in diameter and two and one-half centimeters in thickness. It was situated a little anterior to the center of the hemisphere, and did not anywhere encroach upon the cortical substance. The contiguous brain substance was softened for a thickness of about two lines, but the clot was removed almost entire, and there was no serum, pus, or other indication of inflammation or of extensive degeneration. No pathological changes could be discovered in the left hemisphere. The fluid in the ventricles was not appreciably increased in amount, although there was more serum upon the left than upon the right side. The velum interpositum and choroid plexuses of the ventricles were highly vascular, the veins being turgid and swollen, and this was more marked upon the left side. The tubercula quadragemina were manifestly degenerated, and presented the appearance described as white softening. This condition was much more evident upon the *left* side, but it was not limited to these bodies. It also extended laterally and anteriorly, involving the corpora geniculata, the posterior and inferior portions of the optic thalamus on the *left* side, and also, to some extent, the floor of the fourth ventricle. A portion of the left optic tract and the adjacent under surface of the thalamus was removed for microscopical examination. This was so soft as to require very careful handling to prevent crushing."

Dr. Linnell kindly sent me a portion of the under surface of the left optic thalamus, which came to me preserved in alcohol. The specimen exhibited a grayish-yellow discoloration, as if fatty. It was placed in a one-fifth per cent. solution of chromic acid, and after a few days was sufficiently hard to be sliced with a razor. The sections were mounted in glycerine, and even those which went through the treatment with alcohol and oil of cloves were again introduced into water and mounted in dilute glycerine.

Incidentally, I wish to say that, for three years, I have been pursuing microscopical studies in the laboratory of Dr. C. Heitzmann, and by repeated trials have become convinced that the mounting of specimens in glycerine is far superior to mounting in Canada balsam or Damar varnish. Comparative mountings in these liquids, especially for specimens of the nervous centers, have resulted in the conviction that the balsam or varnish mounting ought to be wholly abandoned. Unquestionably one, if not the main, reason why our knowledge as to the pathology of the brain and the spinal cord has progressed so slowly for the past twenty years is the mounting in balsam. By this method, the specimens in a short time clear up to such an extent that the minutest details fade, and the specimens become unfit for research with high amplifications of the microscope (800 to 1200 diameters), which are the only possible means of revealing the minutest normal, as well as pathological, features.

All the specimens obtained exhibited a peculiar change of the gray substance. This consisted in the presence of homogeneous, grayish fields of greatly varying size and configuration, mostly with fluted outlines, scattered throughout the gray substance. With lower powers of the microscope, I was satisfied that these shining fields either accompanied capillary blood-vessels, or were distributed without any regularity in the gray substance, or, lastly, represented more or less straight tracts in closely lying parallel or in diverging fan-shaped courses, in the direction of the axis-cylinders. The latter feature was especially pronounced in the neighborhood of the optic tract. (See Fig. 180.)

The shining fields are doubtless in close relation to the capillary blood-vessels, inasmuch as they appeared, by the side of the capillaries, as if in the perivascular space, without at first invading the endothelial coat itself. With advancing degeneration in the neighborhood of the blood-vessels, they also became destroyed to such an extent that the direction of the glistening tracts was the only indication of the course of the former capillaries; though, also, in such tracts, occasionally, a small portion of the original capillary was found imbedded. The numerous straight tracts following the course of the axis-cylinders were evidently due to a degeneration upon a large scale.

Owing to the tolerably high degree of refraction of these fields, my first impression was that a fatty degeneration of the gray substance had taken place. The treatment of the specimens, however, with strong alcohol and oil of cloves at once revealed the fact that these formations could not be fat, for they were not perceptibly altered by those re-agents. A second full proof of their not being fat was the treatment with a one per cent. solution of osmic acid, which we know to be the most trustworthy re-agent for fat, and which should stain the fat black. No such thing occurred in my specimens.

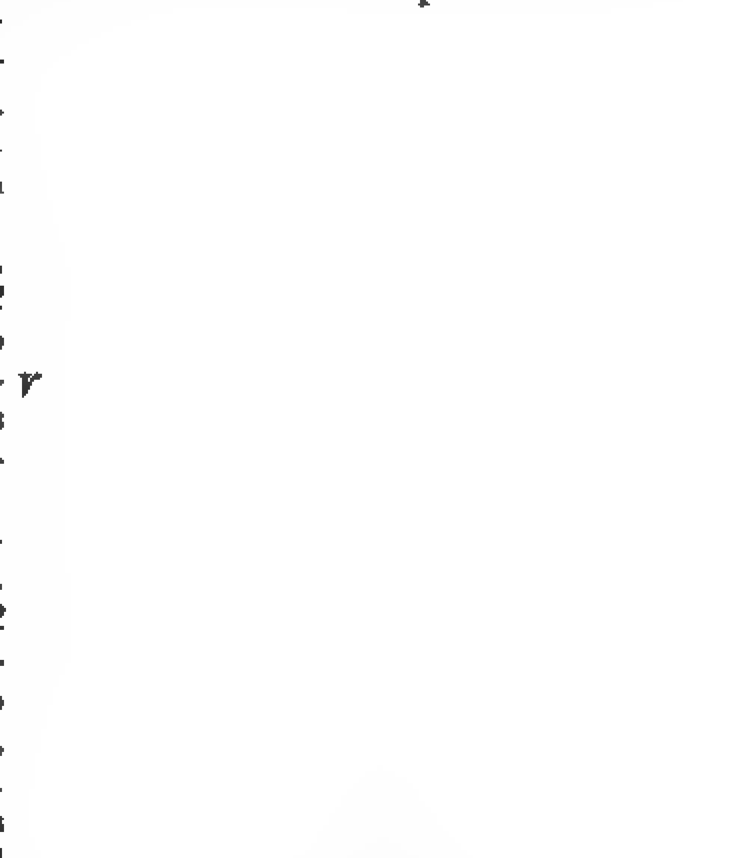


FIG. 180.—WAXY DEGENERATION OF THE GRAY SUBSTANCE OF THE THALAMUS OPTICUS.

V, capillary blood-vessel, containing a granular mass, compressed at its upper portion, surrounded by a layer of the waxy mass, *G*, gray substance, the meshes of the bioplasson enlarged by the waxy material, which collects into branching, irregularly contoured, shining fields, *W*1, *W*2; *N*, nucleus of the gray substance; a part of the periphery, surrounded by a waxy mass. Magnified 900 diameters.

The next question was, could the waxy nature of these fields be proved by the application of different re-agents? To answer this question I applied the following re-agents: Carmine, iodine, hæmatoxylon, fuchsine, violet methyl-aniline, picro-indigo, and chloride of gold. Among those, picro-indigo was the only one which, in Emerson's case, yielded a positive result, where the waxy blood-vessels and globules were rendered by it a bright green. In my case no one of these re-agents, not even the picro-indigo, yielded positive results, as all the hyaline fields remained unchanged in their color.

Nevertheless, I am satisfied that this change is materially a form of waxy degeneration, somewhat different from the degeneration in Emerson's case, but kindred to the waxy degeneration which J. B. Greene * described in the placenta as the most common cause of abortion and premature birth.

* "American Journal of Obstetrics and Diseases of Women and Children," vol. xiii., No. 2, April, 1880.

This certainty as to the nature of this degeneration could be obtained by a study with high amplifications of the microscope, such as 1000 to 1200 diameters. The best specimens for the study with such high powers I obtained by the treatment with a one-half per cent. solution of chloride of gold, in which solution the specimens were placed for one hour and twenty minutes, after having been thoroughly soaked in distilled water. By this, the blood-vessels were rendered dark blue violet, and the gray substance, with its nuclei, purple, while the shining fields remained unaffected. Here I could see the first change into the shining, homogeneous mass before mentioned, at the periphery of the capillary blood-vessels, and in the mesh spaces of the bioplasson reticulum. By the transformation of the liquid contents of a mesh space into a semi-solid shining mass, the space became enlarged, and the neighboring reticulum was pushed apart. By coalescence of neighboring shining formations, larger clusters with fluting outlines originated, in the middle of which often a faint trace of bioplasson was recognizable in the shape of a few delicate granules and their connecting filaments. Whether or not the reticulum of the bioplasson within the homogeneous masses was destroyed, I am unable to say. Not quite infrequently I met with small clusters of the homogeneous mass around nuclei of the gray substance, as if ensheathing them. In the further progress of the degeneration, a great many capillaries became destroyed; probably first by pressure, and later by transformation. These blood-vessels, free of the change just described, looked, especially in their transverse sections, as if compressed and engorged with blood-corpuscles.

My researches prove that there are waxy degenerations going on in the brain-tissue kindred to the waxy degeneration in other organs, such as the spleen, the liver, the kidneys, and the placenta. The intimate reason of this degeneration is not known, nor do we understand its intimate chemical construction. One thing is certainly of interest in the case examined — namely, that the blood-vessels being destroyed to great extent by waxy degeneration, the circulation of the blood in the brain is interfered with, and an encephalitic process may in consequence ensue; or the walls of the blood-vessels, being rendered brittle by the waxy degeneration, may give way the same as in fatty degeneration, and give rise to cerebral hæmorrhage.

XII.

TUBERCULOSIS.*

MY views on the subject of tuberculosis are based on examinations of two hundred corpses in which tuberculosis existed. In a number of these cases death had resulted from other diseases, and tuberculosis was a secondary condition.† A recapitulation of the literature of this subject is found in the excellent book of L. Waldenburg.‡

Nobody who, to-day, undertakes to discuss the question of the formation of tubercle would be allowed to dwell only upon the *theory* of tubercle. On the contrary, he would be bound to consider the former views, and to present the anatomical facts, in order to demonstrate the admissibility of separating the tuberculous granulation from tuberculous infiltration. This cannot be accomplished simply by a description. Rokitansky has settled the descriptive part in such a manner that scarcely anything is left to be said. The views brought forward here are based entirely upon my own observation; they, to some extent, must be eclectic and polemical. An answer to the question what the

* Translated from "Ueber Tuberkelbildung." *Wiener Med. Jahrbücher*, 1874.

† I was able to perform the post-mortem examinations in the dead-house of the Wieden-hospital in Vienna, thanks to the kindness of the curator, Dr. Quiquerez. After the publication of my essay, I made one hundred more examinations of tuberculous bodies, the sum total being, therefore, three hundred.

‡ "Die Tuberculose, die Lungenschwindsucht, und Scrofulose." Berlin, 1869.

nature of tubercle really is can be given only after an accurate examination of facts.

Tuberculosis of the Lungs. In order to properly group the different phenomena of tuberculosis of the lungs, it will be of advantage to first illustrate its four principal varieties.

"Chronic tuberculosis" comprises a tolerably well-defined group, which may be called "localized tuberculosis," as "chronic" is an expression mostly clinical. This form appears most frequently in the apices of the lungs, simultaneously in both, although this is not without exceptions. As it is never fatal, *per se*, we are rarely able to study it as a disease by itself. We meet with it, as an intercurrent condition, in the bodies of individuals dead of other diseases.

We find, imbedded in the lung-tissue, nodules of about the size of a millet- or hemp-seed, which have a gray or grayish-yellow color, are homogeneous, and of soft, or moderately firm, consistency; or we see nodes, the size of a lentil or an almond, distinctly marked from the surrounding tissue. These are circumscribed infiltrations, which, in transverse section, appear almost dry, homogeneous, and of a yellowish-red or yellowish-gray color, which are in firm connection with the adjacent structures, and not yielding juice or tissue-particles on being scraped with the knife. Or, lastly, we find nodules or infiltrations of the size before described, whose centers are usually soft and friable, which can be mashed with the fingers, and from which the scraping-knife can reduce crumbs and brittle particles. In the apices, in some cases, nodules are the only formations present, and these may be found either isolated or conglomerated into groups; in other cases we encounter only nodes, and therefore infiltrations. Not infrequently we see in the same apex a varying number of both nodules and nodes.

All subsequent changes of these formations relate chiefly to the healing process; for, provided that no recurrences take place, localized tuberculosis of the lungs, as a rule, terminates in a cure.

The healing process may be accomplished in two ways. Either it may start in the nodule or the infiltration while they are still in connection with the lung structure, and they themselves represent a tissue, though a morbid one. Or the healing process may start after the nodule or the infiltration have been transformed into a brittle, friable mass, and therefore have ceased to be a tissue.

In the first case, the tubercle is transformed into a semi-transparent or white, consistent, cartilage-like mass (the fibrous tubercle of Virchow), which must be regarded as dense callous connective tissue; or the nodule changes into a firm, dark, pigmented, homogeneous, sometimes stratified, mass—that is, it becomes horny or obsolete. These hard nodules, attaining sometimes the size of a sugar-pea, are often found scattered in the lungs.

If, on the contrary, the disintegration of the tissue has once commenced, the crumbling mass becomes a foreign body, both as regards the surrounding tissue and the whole organism. Here, as around every foreign body, inflammation sets in, and the tissue around it is transformed into a firm connective-tissue capsule, of varying diameter. The encysted product of tubercle becomes a viscid, fatty, sometimes pigmented, paste; or lime-salts are deposited in it, which results in its being transformed into a dry, cement-like mass. Finally, it becomes calcified, and is termed a calcareous concretion.

The tissue in the neighborhood of the diseased focus behaves differently, according to whether originally only discrete or conglomerated, and closely lying foci were present. The surroundings of a horny nodule are found to be lung-tissue, which is radiatingly contracted, but otherwise normal, and from which the hard mass can be easily dug out. The structures in the neighborhood of a callous capsule, on the contrary, are firmly concreted with it, so that the capsule cannot be separated from the inclosing tissue.

If from the very beginning, in a circumscribed district of lung-tissue, numerous nodules and infiltrations are present, and the lung-tissue itself is in the condition of a chronic inflammation, the transformation into a hard, consistent callosity takes place, more or less extensively, usually in the apices of the lungs. The tissue is indurated, and, as it is almost constantly provided with an abundant supply of dark pigment, the callosity appears of a slate-color, or even black. This is the *pigmentary induration* of Virchow, the *cirrhosis* of Corrigan and Buhl.

In the indurated lung-tissue are found all the before-mentioned methods by which tubercle is healed—viz.: the white, almost cartilaginous, nodule, the size of a hemp-seed; the gray or black node of a concentric striation; the cement-like or calcified mass, directly imbedded in the callosity.

Observation, therefore, teaches that a genetic separation of the tuberculous nodule from the tuberculous infiltration is not admis-

sible; that the later metamorphoses depend materially upon the circumstance whether or not the nodule or node remained a tissue; and, further, that the possibility of a focus becoming callous depends greatly upon its size; and, lastly, that the solidification of the lung-tissue may take place either by the formation of a capsule, or as a diffuse induration, and any of these are secondary occurrences.

A second group, found most frequently in bodies of persons who died of tuberculosis, is called *subacute tuberculosis*. As the term "subacute" is mostly a clinical expression, we might term this from the *disseminated or dispersed tuberculosis*. Its characteristic feature is, that new tuberculous nodules and infiltrations are produced in comparatively short space of time, in consequence of repeated recurrences.

If the ulcerative destruction has not reached a high degree, we find almost constantly the first form of tuberculosis, as a general thing, in the apices of the lungs. Upon examining an apex, not too much destroyed, we notice that, while the horny and calcareous nodules remain unchanged, the capsule originally inclosing a friable product has undergone marked alterations. In the transverse section of the callosity constituting the capsule we find gray, grayish-yellow, or yellow nodules, the size of a poppy- or hemp-seed; the inner surface of the capsule is lined with a firmly attached, grayish-yellow, layer, resembling croupous formations. After the removal of this, the intensely reddened capsular wall is seen dotted with the before described nodules. Many of these are in a process of softening, or disintegration into a cheesy, friable mass.

When numerous nodules were originally formed in the callosity, the inflammation accompanying the disintegration evidently leads to suppuration, local mortification, and ulceration of the capsule. The bordering formation of new callous tissue in the inflamed lung-tissue is scanty. Here and there a new rudimentary capsule may appear; or it altogether may be absent where the disease is of rapid course, and then we find lung-tissue, which is eroded, uneven, sinuous, and studded with granulations. Consequently, we meet with transitions from an acute inflammation of the capsule of a tuberculous focus to its suppuration, and to a partial new formation of a thin, so-called pyogenous membrane, and, finally, to an ulcerative destruction of the lung-tissue.

Simultaneously an exudation takes place into the cavity, and the crumbly contents are saturated with the liquid. Should sup-

puration ensue on the inner surface of the capsule, which is freely vascularized, the pus mingles with the former contents, and a thin, serous pus results, which contains a number of friable particles. This is the so-called *tuberculous pus.* At length the entire mass becomes softened, and the formation of a cavity follows, which is inclosed by a capsule and is therefore a closed abscess. The cavity may be completely surrounded by lung-tissue, thus producing the so-called parenchymatous cavity. If a cavity arises from a bronchus by a formation of tubercles in its mucous lining, or if perforation takes place into one or more bronchi, a bronchial cavity is formed, which result must follow after a certain size of the cavity is reached. By this means, the expectoration of the contents becomes possible, and, also, the access of atmospheric air to the contents of the cavity.

The walls between two or more cavities may be perforated by ulcerations, due to a continuous or repeated formation of tubercles. Lastly, a cavity may arise from the confluence of a number of cavities, of sizes varying from that of a walnut to that of the fist of a child or the fist of a man, the walls being formed by lung-tissue, which is partly callous, partly sinuous and corroded.

I would mention, incidentally, that not infrequently the cavity is traversed by firm cords of different sizes, and the walls thickly set with such formations. These are the remains of the former blood-vessels of the lung, which, by thickening of their adventitial coat, have become callous, and resisted the process of ulceration. Sometimes, as is well known, a tuberculous nodule, imbedded in the adventitia, may disintegrate before obliteration of the vessel, and, in consequence of the ulcerative destruction of the wall, a profuse or fatal hæmorrhage may ensue.

Finally, it may happen, perhaps, under the influence of the penetrating air, that a rapid ulcerative destruction invades large portions of the wall of the cavity, which becomes necrosed and, together with the neighboring tissue, passes into gangrene. Then we find the cavity bordered by lung-tissue, of a grayish or brownish-green color, eroded and containing irregular sinuses, while its contents are an offensive, putrescent ichor, mixed with blood, pus-flakes, and cheesy crumbs. These characteristics correspond to the tuberculous phthisis of Laënnec. This term may be employed if we understand by it the ulcerative destruction of the lung-tissue, and if, by the addition of "tuberculous," we designate the nature of the destruction.

In addition to the above-described changes taking place in the neighborhood of the encysted or disintegrated foci, morbid processes occur in the rest of the lung-tissue, most intense, as a rule, in the upper lobes, while the lower lobes are comparatively little affected. In more or less extensive districts, isolated nodules, the size of a poppy- or millet- or hemp-seed, are observed; first as gray, gelatinous dots in the lung-tissue, this being saturated with a viscid, albuminous exudation. Starting from their centers, the nodules then assume a grayish-yellow color, afterward become yellow, and are finally transformed into a cheesy, crumbly mass, before a capsule or callosity has formed in the vicinity. While the old nodules take part in this metamorphosis, fresh gray ones arise, so that we often find in the same lung all transitions, from the gray to the yellow, and disintegrated tuberculous nodule. Sometimes the nodules are grouped around a bronchus in a wreath-like arrangement (Peribronchitis nodosa, Buhl), or they may appear first at the periphery of a lobule which is in the condition of a flabby, red, or grayish-red hepatization. They may also fill the whole lobule, retaining their nodular form as long as no disintegration has taken place.

Sometimes only scattered nodules are met with in the diseased lung; sometimes nodules are combined with infiltrations; and sometimes only infiltrations present themselves, which consist of grayish-yellow, firm, half-dry foci, ranging in size from that of a lentil to that of a hazel-nut, such as I have described as occurring in chronic tuberculosis.

The infiltrations become disintegrated into a friable, crumbly mass. This disintegration always starts from the centers of the diseased parts. The view held by older pathologists, and also by Virchow, is that the softening is a chemical process, occurring, perhaps, independently of any imbibition of water from without. This idea of a melting process taking place, as it were, in the own liquid, follows from the belief that the infiltration from its very outset appears of a certain size, and retains this size until "melted" or transformed to "softened cheese." A different explanation may be obtained if we remember the fact that the node at its periphery continues enlarging, and that the oldest focus of disease is to be looked for at the place where the softening starts. The tuberculous mass, therefore, may have become soft by liquid derived from the inflamed neighboring parts before peripheral new production has occurred, which still exists in the "cheesy" stage.

Softened infiltrations are usually bounded by thin, yellow, sinuous layers of tissue. In the vicinity the lung usually appears in the state of flabby, red hepatization, saturated with a viscid exudate, and at other times it is moderately indurated. The softening of the infiltrations also terminates in the formation of cavities, and the ulcerative destruction of the lungs. This variety of tuberculous phthisis differs from that described before only in form and acuity, but not in any essential point, nor in its terminations.

Sometimes, scattered or clustered nodules and infiltrations fill a district or the larger portion of a lobe so entirely that this becomes rigid, fragile, and, in part, atelectatic. In such cases, we may speak of a *pneumoniform, subacute tuberculosis*, whose features are sufficiently marked to distinguish it from catarrhal or "desquamative" pneumonia. If a group of nodules, or an infiltration lying close to the pleura, is disintegrated, and the pleura destroyed by ulceration, perforation into the pectoral cavity may follow. This is the most common cause of pneumo- and pyo-pneumothorax, which not infrequently accompany tuberculosis of the lungs.

In looking over the second form of tuberculosis of the lungs, we again are satisfied that there is no essential difference between a nodule and an infiltration; that either may be transformed into a crumbly mass and become softened. The next step—i. e., *ulceration of the lung-tissue—is different only in its acuteness; that is, according to whether a number of scattered nodules are breaking down at different times, or whether an infiltration is continually softened and simultaneously increases in size at its periphery. The surrounding lung-tissue, in all forms of softening and local necrosis, is evidently involved only in a secondary manner, therefore is in a "re-active," acute, or chronic inflammation.*

The third form of tuberculosis of the lungs is comparatively rare; it is called *tuberculous pneumonia, pneumonia tuberculisans*. In the description of subacute tuberculosis, I have already mentioned that lobules, in flabby hepatization, are sometimes the points where tuberculous nodules or infiltrations are formed. Should this grayish-red or gray hepatization involve a number of lobules, or nearly the whole of a lobe, the features of *lobular pneumonia* arise. It becomes tuberculous by the appearance of gray and grayish-yellow nodules, or of gray and grayish-yellow infiltration, either in the neighborhood of bronchi or at the periphery of the lobules, or scattered throughout them. In the

initial stages of the disease the infiltrations are not sharply marked from the surrounding hepatized lung-tissue. Sometimes they have the appearance of being composed of numerous conglomerated particles the size of a pin's point.

At other times we find a lobe, or the larger portion of a wing, in the condition of *lobar pneumonia*, consequently enlarged, heavy, dense, rigid, and without air—*i. e.*, in a grayish-red or gray hepatization; and if the inflammation has invaded a pigmented lung, it has the aspect of granite.

In genuine croupous pneumonia the section looks finely granular, owing to the filling of the alveoli; if the inflammation has attacked a coarsely spaced, atrophic lung, it is filled with coarser, yellow exudation plugs. In tuberculous pneumonia, on the contrary, we find, usually, in the vicinity of the finer bronchi, groups of moderately firm, grayish-yellow nodules, in varying numbers, imbedded in the hepatized tissue. I have observed this form several times, generally in the lower lobes, after capital operations—f. i., amputations in individuals who, by previous suppurative processes, had become broken down.

In a third instance we find the whole wing in brown-red hepatization, its tissue without air, firmly indurated with a slight serous infiltration, and pervaded by numerous nodules the size of hemp-seed, or nodes from the sizes of a lentil to that of a hazelnut; these are mostly softened. Such a lung exhibits an aspect similar to that of porphyry. If the indurated tissue of the wing is profusely pigmented, the pigmentary induration, therefore, has invaded the whole wing, we find in it scattered nodules, usually of a size not exceeding that of a millet- or hemp-seed, which may be both obsolete and calcareous, or gray, grayish-yellow, and soft. Here, too, the characteristics of pneumonia are marked and have led to a condensation, hypertrophy, callosity, and pigmentary induration. Still the nature of the process is sufficiently apparent by the presence of the nodules and infiltrations.

Finally, we find in the indurated tissue of red-brown hepatization of which only little is left, firm, grayish-yellow, half-dry infiltrations, partly softened, about the size of a pea, hazel-nut, or perhaps as large as a walnut, which are closely packed together or confluent. An entire lobe, or wing, with the exception of scanty remains of red-brown, hepatized lung-tissue, may be pervaded by this "cheesy" infiltration, which on being scraped yields only a small amount of a cloudy liquid. Such an infiltration renders the diseased tissue friable and brittle. Only the

pigment indicates the otherwise unrecognizable lung-tissue (Rokitansky).

One of the cases which I observed deserves mentioning, because it will be of value in supporting the theory of tuberculosis, to be dwelt upon later. A strong boy, æt. 15, was taken to the hospital with the symptoms of typhoid fever. Soon pneumonia of the right lung was diagnosticated. Two months afterward the patient died, with symptoms of a clinically diagnosticated tuberculous pneumonia. In autopsy I found the right wing pervaded by "cheesy" infiltrations to such a degree that the tissue was atelectatic and firm; the left lung at its apex contained an infiltration the size of a child's fist. The infiltrations in both apices were softened, and in the right apex showed a number of cavities of different sizes, but not very large. No traces of any previous chronic tuberculosis could be discovered. The spleen, the small intestines, and the mesenteric lymph-ganglia had the same appearance as seen in typhoid fever after the healing process had been going on for a few weeks. Here, therefore, under the influence of marasmus after typhoid fever, an original, clinically well-marked genuine pneumonia was changed into a tuberculous pneumonia.

The nodules and infiltrations, through their peculiarities, may be at once recognized as tuberculous, because they are markedly different from analogous nodular infiltrations of the lungs, as observed in carcinomatosis and pyæmia. The distinguishing features are: the white color, the scanty vascularization, the wreath-like arrangement around the pulmonary vessels in carcinomatosis; the yellow color, the softness, the partial disintegration to pus or ichor, the purple color, and sometimes the dark red hepatization of the neighboring parts in pyæmic infarctions.

A fourth form of tuberculosis of the lungs is known by the name of the *acute or miliary tuberculosis* (Bayle). Here we find both lungs diseased nearly simultaneously, and to nearly the same extent. They are enlarged, heavy, profusely supplied with blood, and saturated with a viscid, cloudy exudate. In the apices we encounter chronic and sometimes even healed tuberculosis; in other cases, no trace of this condition. The whole hyperæmic lung-tissue is pervaded in nearly uniform distribution by more or less densely arranged gray, or grayish-yellow, soft, translucent, opaque nodules, the size of poppy-, millet-, or hemp-seed. In several cases, the largest and most numerous of these nodules were found in the upper lobes; comparatively few nodules of the millet-seed size in the right middle lobe, and but very few gray nodules the size of a poppy-seed (submiliary) in the lower lobes. All cases of this variety exhibited in the meninges, the liver, the spleen, the kidneys, and the peritoneum the same morbid conditions in different combinations.

Beyond this stage no changes are observed, for this form of the disease, as a rule, terminates fatally, with symptoms similar to those of typhoid fever. This form is the rarest. It differs from nodular tuberculosis, termed subacute, only in the simultaneous appearance of tubercle nodules in different organs and the acuteness of its course. I can corroborate, from my own careful researches, the statement of Buhl that in ten per cent. of the cases dead of this variety of tuberculosis no trace of cheesy focus can be found.

Tuberculosis of the Serous and Mucous Membranes. Under this head I shall only take into consideration tuberculosis of the pleura and the peritoneum, as these have supplied me with the most abundant material for observation.

In the pleura, we find tuberculosis is always combined with the chronic or subacute form of the disease in the lungs, and in the peritoneum also, though here not so constantly, it is found secondary to tuberculosis of other organs. This form of disease has features corresponding with those of chronic tuberculosis of the lungs, and may be considered as *chronic tuberculosis of the pleura and the peritoneum.*

The pleura of one pectoral cavity, and the parietal peritoneum in its whole extent, may be considerably thickened, and transformed into a white, firm, and dense callosity. I have seen the peritoneum in the pubic region as thick as the width of the little finger. These callosities were either formed by the costal, diaphragmatic, and the pulmonary pleura, or, as is sometimes the case, mostly by the costal pleura alone. In the abdominal cavity the thickened parietal layer was concreted with the visceral layer by means of thin, pseudo-membraneous cords and plates. In the callosity I found abundant foci, from the size of a hemp-seed to that of a hazel-nut, containing a crumbly mass. In the pleura I met even with cavities, ranging from the size of a hazel-nut to that of a pigeon's-egg, which were filled with a mixture of pus and cheesy particles. I could trace all transitions in consistence and liquefaction, from cheese to pus. I have several times encountered such foci between the basis of the lung and the diaphragma, and also at the anterior border of the lung, with perforations outward, between the third and the fourth rib. I have also observed this condition at the posterior border of the lung, in the niche formed by the union of the vertebræ and ribs, with caries of single ribs. In the peritoneum I have observed such cavities perforating into the abdominal space, with subse-

quent ulceration of the pseudo-membraneous adhesions, between the parietal and visceral layer, and a final perforation of the intestine from without inward.

That tuberculous nodules of the peritoneum, however, may heal up in the same way as those of the lungs is proved by cases in which the small intestines are found massed together and thickened, and at the periphery surrounded by a thick, pseudo-membraneous capsule. Upon detaching the firmly agglutinated loops, the visceral peritoneum was found strewn with nodules, either isolated or in groups, of the size of a millet- or hemp-seed. They were colorless, half translucent, and sometimes transparent, having a vesicular appearance; or they were white, firm, fibrous, even cartilaginous, while many of the nodules and clusters were surrounded by a narrow area of dark brown or gray pigment.

I have sometimes found, in the peritoneum, a second form of tuberculosis, of a subacute character—*i. e.*, a miliary tuberculosis—with repeated recurrences. The conditions were the following: after opening the abdominal cavity, which was filled with a serous or hæmorrhagic exudation, I saw in both peritoneal layers, besides firm nodules encircled by pigment, others which were of a grayish-yellow or yellow color, surrounded by an injected or hæmorrhagic area, and still other nodules which were gray or grayish-yellow in color, tolerably soft, easily mashed, and imbedded in the cloudy, swelled peritoneum. Scarcely a doubt could arise that, in such cases, the "fibrous" and pigmentary nodules were the oldest, or they might even be healed, judging from their analogy to the "obsolete" or "cartilaginous" nodules of the lung, and also from the fact that pigment can form only after a certain length of time. That, however, repeated recurrences had taken place was proved by the presence of tuberculous nodules in their different stages, such as we have become acquainted with through the researches of Laënnec.

A third form is the *acute, miliary tuberculosis of the pleura and the peritoneum*, which is always combined with tuberculosis of other organs. We find the pleura and the peritoneum thickened by pseudo-membraneous layers and pervaded by innumerable tubercles, which, in some parts, are isolated and in others coalesced. Some of these are mere dots, the size of a pin's point, and others are as large as a millet- or hemp-seed. All of them show a nearly uniform grayish-yellow or yellow color. Pseudo-membraneous callosities of varying thickness may be throughout crowded with yellow tubercles, which have, to a great extent,

become confluent, and in some localities are packed together without a trace of separating tissue. The same condition may be observed in the omentum after it has grown together into a firm, bulky mass. Sometimes there are present simultaneously recent, cobweb-like, freely vascularized pseudo-membranes, which may be crowded with submiliary gray tubercle granules, not surpassing in size a pin's point.

Of the mucous membranes I shall consider only the mucosa of the larynx, the intestine, the uterus, and its tubes. The different forms of tubercle cannot be traced in mucous membranes, because the nodules and infiltrations lie near the surface and rapidly soften, disintegrate, and lead to ulcerative destruction of the mucosa.

Doubts have been raised (Rheiner) whether or not *the ulcers in the posterior wall of the larynx*, which are so often combined with tuberculosis of the lungs, are really tuberculous in nature. As is well known, they are either follicular or cleft-like, either shallow and superficial, or sinuous ulcers, which, penetrating into the depth, sometimes cause necrosis of the cartilages of the larynx. All doubts regarding the tuberculous nature of these ulcers will disappear if we see—though not in many instances, it is true—in the mucosa of the larynx, at the borders and the basis of the ulcers, yellow, flat infiltrations, the size of millet- or hemp-seed.

The mucosa of the lower ileum, the cæcum, the ascending and transverse colon, offer a good chance to study, macroscopically, the genesis and the course of tuberculosis. Not infrequently we see intestines in which there are all transitions, from minute, follicular nodules and superficial ulcers, springing from them to an ulceration, extending over several square inches in circumference, the so-called tuberculous phthisis of the intestine.

The formation of tubercles, and the consequent ulceration, is sometimes *chronic* and sometimes *acute* in its course (Rokitansky). I would mention here that the deepening and spreading of the ulcers is due to a continuous new formation of tuberculous nodules, which are seen as flat, grayish-yellow, and yellow formations, the size of hemp-seeds, imbedded in the inflamed tissue. In the chronic course of tubercle formation a thickening of the mucosa and of the sub-peritoneal tissue takes place, in the neighborhood and at the base of the ulcer. The ileo-cœcal valve may remain as a ledge-like projection, of several lines in thickness, of considerable density, and undermined by a number of sinuous ulcers, emptying above and below the valve.

When the ulceration penetrates the sub-peritoneal tissue, a circumscribed peritonitis always follows, corresponding in extent to the size of the ulcer. This peritonitis is decidedly marked by nodules, which are either discrete or grouped together in clusters, of a yellow or grayish-yellow color, and are imbedded in the tissue of the peritoneum, which is swelled, opaque, and often considerably injected and ecchymosed. Such an acute localized formation of tubercles, accompanied by considerable hyperæmia of the peritoneum, may give rise either to a peritonitis confined to the hypogastrium, or to a general purulent peritonitis. Finally, if in the peritoneum tubercle, in circumscribed places, is softened and disintegrated, and if no protecting pseudo-membrane has been previously formed, a perforation of the wall of the intestine will take place, with an escape of the contents into the abdominal cavity, and a general purulent peritonitis will set in, with a rapidly fatal termination. *Tuberculosis of the mucosa of the uterus and the tubes* exhibits similar characteristics. Here, too, the primary tuberculous formation appears as flat, gray, or grayish-yellow granulations, which are only exceptionally found in the mucosa of the fundus uteri and that of the swelled and winding tubes. I encountered most frequently ulcerative destruction of the mucosa to a considerable extent. These ulcers were shallow, and were defined by abrupt, sinuous, and irregularly eroded borders. Upon removing the cheesy, crumbly, and sometimes almost as if croupous, formation from the surface of the mucosa, flat, grayish-yellow infiltrations about the size of hempseed became at once visible. Real nodules are of as rare an occurrence in this situation as in the mucosa of the larynx; for the prominence, which is the essential feature of a nodule, is wanting.

Tuberculosis and Scrofulosis of the Lymph-ganglia. O. Schüppel* has arrived at results widely different from those of Virchow. He admits the fact that there exists such a thing as primary tuberculosis of the lymph-ganglia, and that this may arise and terminate as a purely local disease. He describes the tubercles of the ganglia as "globular, tolerably well-marked nodules of not more than O. 3 mm. diameter, which are invariably and exclusively located in the vascularized follicles of the ganglion." Schüppel also considers only the nodules to be tubercles, and, in his opinion, scrofulosis is nothing more than a miliary tuberculosis of the inflamed hyperplastic ganglion. This conception I cannot accept as correct. True, sometimes we meet with

* "Untersuchungen über Lymphdrüsen—Tuberculose," 1871.

nodules—*i. e.*, prominent formations of a size varying from that of a pin's point to that of a hemp-seed—in ganglia which are swelled, softened, and grayish-red. More commonly, however, such nodules are wanting, and the diseased ganglion exhibits a grayish-yellow discoloration, either throughout the transverse section or only in a portion of it, and in the latter case the discoloration is sharply marked from the gray-red, vascularized portion of the ganglion. If a discoloration is observed in a submiliary spot the size of a pin's prick or of a poppy-seed without a protrusion, what reason have we for calling it a "nodule"? Would it not be more correct to name such a condition an "infiltration"? If we observe whitish-yellow submiliary spots on a grayish-yellow basis, are we authorized in calling only the whitish-yellow parts tubercles? And, lastly, if the whole ganglion has become homogeneous, grayish-yellow, half-dry and friable, where are the tubercles?

I should say that here, as in every other tissue, a sharp distinction between the tuberculous nodule and the tuberculous infiltration leads to confusion and error, and I should prefer insisting upon the genetic identity of both these forms, also in the lymph-ganglia. I, however, agree with Schüppel in the view that the tubercle is formed from an inflammatory new formation, and that scrofulosis and tuberculosis are identical.

If we should place before a person a lymph-ganglion in "cheesy" metamorphosis, without telling him from what part of the body it came and what were the concomitant phenomena, would he be able to decide whether this ganglion was scrofulous or tuberculous, or whether it came from the region of typhoid or cancerous disease? I should certainly think not. The feature common to all is the grayish-yellow infiltration, the "cheese" of Virchow. Later stages of disintegration, softening, suppuration, or calcification are also identical. Nevertheless, Virchow considered it necessary to separate "scrofulosis" from "tuberculosis."

To what the "cheesy" degeneration is due I will demonstrate later. Here I only wish to maintain that there is no one invariable anatomical sign which would entitle us to call a given ganglion either scrofulous or tuberculous. Schüppel, however, deserves credit for having demonstrated, by the means of microscopic research, that the theory of "hyperplasia" and "heteroplasia" is not tenable, especially so far as tuberculosis of the lymph-ganglia is concerned.

Finally, I would draw attention to the fact that the ganglion in grayish-yellow or cheesy infiltration may become softened and suppurate. This process starts from certain centers, and results in the formation of a "scrofulous" abscess. In an abscess of this kind, the thin pus mixed with cheesy crumbs is so characteristic that the experienced surgeon Schuh at once made the diagnosis of "scrofulosis" in an apparently well-nourished individual, when upon incision the abscess yielded pus of the above description.

On the other hand, the softened infiltration may become fatty and encysted, or calcified, and in the latter case the whole lymph-ganglion in time is transformed to a calcareous mass the size of a hazel-nut, such as we sometimes find in the mesentery.

Tuberculosis of the Kidneys—Concomitant Nephritis. Before entering upon the description of my researches concerning tuberculosis of the kidneys, I would remark that the kidneys here considered were not primarily affected by tuberculosis, but the same pathological condition existed in other organs, notably in the lungs.

Not infrequently we meet, both in the pyramids and in the cortical portion, with single, white, almost cartilaginous infiltrations, of sizes varying from that of a millet- up to that of a hemp-seed, which are surrounded by unchanged kidney-tissue, and, in accordance with analogous occurrences before described, might be considered as *healed tubercles.* Whether or not the firm, yellowish-white, callous nodes, the size of a lentil or a pea, are tuberculous formations is doubtful, for we also see such nodes in the kidneys of non-tuberculous individuals. They might be, with equal reason, considered healed infarctions, more particularly if any evidences of healed endocarditis are found.

Chronic and Subacute Tuberculosis of the Kidneys I have encountered much less frequently than other forms of the disease. I have occasionally seen small, yellow, friable infiltrations in the swelled, cloudy, partly ecchymosed cortex, in the neighborhood of which wreath-like or discrete infiltrations, the size of a millet- or hemp-seed, were found. I concluded, from similar occurrences in the lungs, that the larger infiltrations were the oldest, the smaller ones of a later date, without maintaining, however, that the former originated from the latter. In chronic tuberculosis of the kidneys, tuberculous phthisis may arise from confluence of a number of foci, which, though a simultaneous cal-

lous condensation of the bordering connective tissue takes place, may become softened and produce cavities (Rokitansky).

Lastly, *acute miliary tuberculosis of the kidneys* is observed as infiltrations, not exceeding the size of a millet-seed, which, as a rule, are most abundant in the cortical substance, and present, in a comparatively small amount, in the pyramids. Such formations are either scattered or, in part, clustered together, with simultaneous miliary tuberculosis of the lungs, the peritoneum, and the liver. This form of tuberculosis of the kidneys I have seen but twice.

Here I wish to draw attention to the nephritis which accompanies both the tuberculosis of the kidneys and that of other organs. Usually, many different forms of nephritis are classed under the head of "Bright's disease," and Rokitansky especially distinguishes an acute and a chronic form. I wish briefly to state that, in these two varieties of Rokitansky, I recognize two kinds of inflammation of the kidneys, readily distinguishable as diseases *sui generis*. What Rokitansky describes as acute "Bright's disease" should be designated *croupous nephritis*, a characteristic of which, in addition to the inflammatory swelling and redness or hyperæmia, is a diffused exudation. Rokitansky's chronic form of "Bright's disease," on the contrary, must be considered *an interstitial, catarrhal, or desquamative nephritis*.

In *croupous nephritis* tubular casts appear in the urine, and large quantities of albumen, and the casts are recognizable even after waxy degeneration of the kidneys has ensued. In *catarrhal nephritis*, on the contrary, there is albumen in the urine in a comparatively small quantity, the tubular casts are missing, and only desquamated epithelia of the uriniferous tubules are found. It is obvious that these forms of inflammation are different only in degree and not in acuteness. Catarrhal nephritis may also appear in an acute form and be followed by acute recurrences, in which, as a rule, the urine becomes more albuminous.

The characteristic pathological sign of catarrhal or interstitial nephritis is the striation of the sometimes slightly, sometimes considerably, swelled cortical substance. The striation is most marked on the boundary line between the cortical and pyramidal substances. The seat of the disease is evidently the connective tissue between the uriniferous tubules, while the exudation into the tubules leads only to a desquamation of the epithelia, but not to formations similar to those of croup of mucous membranes. In acute catarrhal nephritis and in its acute recurrences there

are gray striations, alternating with the dark brownish-red hyperæmic kidney-tissue and the engorged blood-vessels. In the chronic form of this disease, on the contrary, the striation is of a grayish-yellow color, and there is no hyperæmia whatever of the kidney-tissue.

One of the reasons which led to the statement that these two varieties are different morbid conditions, was the difference observed in the appearance of the consecutive atrophy. After croupous nephritis this appears on the surface of the kidneys as a coarse lobulation, with the formation of irregular elevations and depressions of the cortical substance; while after catarrhal nephritis there is only a more or less uniform granulation and shallow furrowing of the surface. The most striking proof is furnished by kidneys which were in both poles in part attacked by catarrhal and in part by croupous nephritis. The parts in catarrhal inflammation exhibit fine granulation on the surface and corresponding grayish-yellow striation of the nearly uniformly reduced cortical layer. In the portion attacked by croupous inflammation the surface is coarsely lobular, and a grayish-yellow infiltration prevails in both the irregularly atrophied cortical and the reduced pyramidal layers.

In the highest degrees of atrophy after catarrhal nephritis the kidney is uniformly reduced to a half, a third, or even less, its original size, yet still there is an indication of the striation of the narrowed cortex, which blends, almost without a boundary line, with the striated pyramids. The granulation of the surface is very marked. After croupous nephritis in the highest degrees of atrophy there are large nodes, separated from each other by deep furrows, with an almost complete destruction of the cortical substance, and also a marked reduction of the pyramids, which are pushed apart. In addition, there is a considerable amount of fat at the periphery, and also at the hilus of the kidney, and a more or less marked secondary waxy degeneration of the kidney-tissue, which in some places may be reduced to a diameter of not more than four to five lines.

In both forms of nephritis, however, *fatty* and *waxy degeneration* occur. Fatty degeneration in either produces a diffuse yellow discoloration of the kidney, and for the recognition of the original morbid process the increased volume of the organ and the aspect of its surface are decisive. I have observed high degree of waxy degeneration after both kinds of nephritis, but so far as my subjects of observation admit of a conclusion, I

should say this condition was less frequent after catarrhal than after croupous nephritis. In the first instance, the waxy degeneration invades a pale or dark-brownish-red kidney, or it may be confined to the pyramidal substance only; while in the last instance the lardaceous appearance is uniformly distributed throughout the organ.

Out of two hundred cases of tuberculosis of different organs I found croupous nephritis only seven times. In bodies, on the contrary, in which tuberculosis was the cause of death, I have never failed in finding catarrhal nephritis. I am far from connecting nephritis in causal relation with the tuberculosis of other organs. Catarrhal nephritis almost invariably accompanies all severe acute and chronic diseases — f. i., croupous pneumonia, typhoid fever, small-pox, pyæmia, chronic suppurative processes, etc. Besides, both forms of nephritis may appear primarily with the well-known symptoms, and in their severest forms lead to a fatal termination.

Theory of Tuberculosis.

Anatomical Signs of the Tubercle. We must examine the characteristics of the morbid process which are concerned in the formation of tubercle: the features which are observed by the naked eye, those brought to light by the microscope, and those inferred from the views taken by different pathologists. In this way we may obtain a definition of the tubercle.

What are the characteristic features of tubercle?

Is it the nodular shape? Certainly not. We know of a number of diseases of the skin which are characterized by nodules, such as lichen, milium, acne, etc., and all follicular furuncles are at first nodular. We know that in catarrhal inflammation of the mucous membranes nodular follicular swellings occur, which disappear as soon as the inflammation subsides. Occasionally we find, in corpses where there is no sign of tuberculosis, nodules the size of a pin's point or a poppy-seed, in the peritoneal covering of the liver and spleen, and sometimes, also, in the pleura. These are very firm, transparent, without an injected area, and are located on slightly cloudy or unchanged bases. Their origin is apparent to any one who has seen acute pleuritis, especially in the neighborhood of peripheral pyæmic infarctions of the lung, and acute peritonitis in its earliest stages—f. i., in puerperal process. Further, we often encounter, chiefly at the free

border of the bicuspid valve, nodules the size of a millet- or hemp-seed; these are sometimes pedunculated, and are papillary vegetations from former endocarditis. Lastly, a number of tumors, fibroma, papilloma, sarcoma, and cancer appear, first as a nodule. Who would think of designating such nodules tubercles, although they are in reality "*tubercula*"?

Is it the form of an infiltration? We have no better grounds for that. The swelled patches and solitary follicles of the mucosa of the intestines, the enlarged bronchial and mesenteric lymph-ganglia in typhoid fever, pyæmic infarctions of the lungs, etc., furnish examples of circumscribed infiltrations; in croupous pneumonia and in croupous nephritis we have specimens of diffuse infiltrations, and such infiltrations, it is obvious, have nothing in common with tuberculosis.

We, therefore, look in vain for the shape to distinctly characterize the disease termed tuberculosis. *Not only tuberculosis, but any product of inflammation, may appear at one time as a nodule, at other times as an infiltration.* Let us search further for a pathological feature peculiar to this disease.

Is it the cheesy metamorphosis? We know, on the one hand, that tuberculous nodules do not always pass on to this metamorphosis, as is demonstrated by the isolated "fibrous" tubercles of serous membranes, whose cure is made manifest by the pigmentary area and by the obsolete nodes of the lungs, which, as mentioned before, sometimes attain the size of a sugar-pea. We know, on the other hand, that the tissues of cancer, of typhoid lymph-ganglia, nay, pus itself, may undergo a cheesy metamorphosis. Virchow announced that a tissue might, under some conditions, become caseous, as it might under other conditions enter calcareous, fatty degeneration or become putrescent. According to his view, there is a hyperplasia which terminates into a caseous condition (scrofule of a lymph-ganglion) and a heteroplasia which also terminates in the same caseous change (tubercle, cancer). This "cheesy" change, therefore, cannot be an essential feature of tubercle.

Is it the heteroplasia? In Virchow's classification the miliary tubercles belong to the lymphatic tumors; they are adenoid—*i. e.*, gland-like new formations and *heteroplastic productions*—which means that they originate "in places in which they do not belong." I cannot think that Virchow intended this for a serious definition. We know perfectly well that any inflammatory new formation, without exception, any "accumulation of cells," may

be of a "lymphoid" character,—f. i., the granulations of a wound, —and very likely every disease does originate in a place where it does not belong. Besides, Schüppel *(l. c.)* has demonstrated that the view of a "heteroplastic" origin of the tubercles of the lymph-ganglia is not tenable.

More recently, efforts have been made to locate the essential sign of the tubercle in its *multinuclear elements*—Rokitansky's mother-cells. In this view, the presence of a central "multinuclear cell" would be sufficient to stigmatize all the surrounding "lymphoid" new formation as tuberculous. We know that the so-called "giant-cells" occur, not only in normal medullary tissue of bone and in inflamed tissues, such as cornea, cartilage, bone, but also in a number of tumors (sarcomata), so that it is impossible to consider them as definite characteristics of the formation of tubercle. They are no more specific for this disease than are the "tubercle-cells" of Lebert.

Neither are we justified in claiming that the minute size of the elements, their transient nature, their "low vitality," are characteristic. The so-called "small-cellular" sarcomata and cancers in disintegration exhibit elements which are certainly still less stable than those of the tubercle. Besides, we find in the tubercle the large, so-called epitheloid, and also the very large multinuclear elements.

This much is certain, that all previous definitions of tubercle lack clearness. I again return to the question, what are the essential characteristics of tubercle?

Beyond doubt (and on this point all observers are agreed) the tubercle is a new formation—*i. e.*, a new product "in a place where it does not belong." It, however, has a peculiarity known to all accurate observers. *It contains no blood-vessels. Tubercle, therefore, is an avascular new formation.*

Origin of Tubercle. As early as 1816 Broussais maintained that the tubercle, or rather the "tuberculous matter," was a product of inflammation. Much discussion followed this assertion, but all was to no purpose, since nobody then knew what inflammation really was. Most later observers have considered the pneumonic form of tuberculosis of the lungs as inflammatory in nature, and even Virchow cannot be suspected, having considered every tuberculosis due to inflammation.

While Broussais took "irritation" and "inflammation" for one and the same process, Virchow, in a logical manner, separated them. He says: "Primary tuberculosis of the lymph-glands

is primary only as tuberculosis, but not as a process of irritation, whose irritating agency is generally carried in from an *atrium*." This ingenious remark shows that the irritating agency is to be considered as the cause—the irritative process, on the contrary, as the result. The difference between the "irritation" of Broussais and the "irritative process" of Virchow is obvious.

The history of the theory of inflammation elucidates the meaning of the process under consideration. Humoral pathology placed it almost exclusively in the blood-vessels and in the diseased blood. Cellular pathology, on the contrary, set aside the blood-vessels and everything arising from the blood, and sought for the essentials in a disease of the tissue, in the inflammatory new formation. To the irritating agency at first the blood-vessels only responded; later, only the cells of the tissue.

S. Stricker, in 1870, in opposition to these views, urged the importance of the blood and the blood-vessels as factors in giving rise to the inflammatory process; and he demonstrated that the blood-vessels take an essential part in the production of tissue changes.

Since then, somewhat more has been added. It is proved through my own researches that, besides the exudation and the new formation of living matter, the *new formation of blood and blood-vessels* is an essential feature of traumatic inflammation. I have shown that the process of inflammation first causes a liberation of the living matter, which before was infiltrated with basis-substance; that the inflamed tissue first returns to its juvenile or embryonal condition, and that it splits up in the primordial elements from which it originated. The "inflammatory cell-infiltration," therefore, must be regarded only as the representative of an early normal condition. A real "inflammatory new formation" does not take place till later, when the living matter is newly formed and the elements divide in boundaries, depending upon the more compact centers, the nucleoli and the nuclei.

Rokitansky, in 1854, ascertained that the "tissue-cells" are not by any means the only starting-points of inflammatory new formation, but in the outgrowth of connective tissue the "intercellular substance" also participates actively. I demonstrated in 1873 that the basis-substance of all varieties of connective tissue is abundantly supplied with living matter, and that after a dissolution or liquefaction of the glue-yielding basis-substance the living matter is productive as well as the cells. I have therefore

supported the views held by Rokitansky, in opposition to the plasma theory of Schwann and the cell-proliferation of Virchow. The substratum of the inflammatory new formation, the outgrowth of connective tissue, is the whole of the living matter of a living tissue.

This process, as before mentioned, is constantly accompanied by a new formation of red blood-corpuscles and also of blood-vessels, due to a new formation of living matter. This occurs in all tissues formed from the middle germinal layer, which from their very origin are supplied with blood and blood-vessels.

The result of these processes is *the formation of a new tissue, which simultaneously becomes vascularized,* such as granulations, vegetations, pseudo-membranes, etc. Virchow is satisfied in the belief that a "tissue" is a mere accumulation of "cells"; while I have proved that we are justified in applying the term "tissue" only when the elements are in a continuous living connection. Isolation of the elements produces pus; pus is not a tissue, and not endowed with the capacity for forming a tissue.

The fact has been known a long time that inflammation may exhibit marked differences, both in its course and in its terminations. "Acute" and "chronic," "sthenic" and "asthenic," "plastic" and "suppurative" inflammation are expressions common to all clinicians. One of the most striking differences in the course of inflammation was based upon the circumstance that, in some instances, the disturbance is mainly confined to the vascular system, in others it mainly appears in the inflamed tissue itself. One of the main supports of the theory of the cellular pathology was that the phenomena of vascular disturbance, nay, the blood-vessels themselves, might be absent,—f. i., in the cornea or the cartilage,—and, notwithstanding, the tissue could become inflamed. A new formation of "cells," even suppuration, might occur in such tissues, these results being sufficient for the diagnosis of an inflamed tissue. The essential feature of inflammation was the new formation of "cells." To-day, things are different. With us, a new formation of "cells" means a new formation of living matter, and we are satisfied that blood and blood-vessels are requisite to set up an inflammation. We know, besides, that in inflammation a number of blood-vessels perish, their hollow bioplasson becomes solid and is immediately appropriated for the new formation of tissue; while a simultaneous formation of blood-vessels is going on by the hollowing and vacuolation of originally solid cords of living matter.

One fact only remains to be considered—namely, that on the one hand the phenomena in the vascular system, under certain circumstances, may be slightly marked, and on the other hand the new formation of living matter may be comparatively so scanty that in the inflamed district a new formation of blood-vessels is completely absent. With this knowledge we may undertake to analyze tubercle—it is immaterial whether in the form of a nodule or an infiltration.

Tubercle arises in vascularized tissues only. The inflammatory phenomena in the vascular system in the initial stage of forming nodules are not marked to the naked eye, but are rather more distinct in the formation of an infiltration.

Tubercle, for the cellular pathologist, is a tissue composed of proliferated and divided "cells"; with us, it is bioplasson freed from basis-substance, with a scanty new formation of living matter. This explains the gray color and the softness of a fresh tubercle nodule.

Tubercle, furthermore, is a tissue which is connected with the mother-tissue, and in which all elements are in a living union, established by the connecting filaments.

Tubercle is composed mostly of small elements, as there are only small centers of living matter—viz.: small nuclei and nucleoli.

Finally, tubercle is avascular; in other words, in the production of the tissue of the tubercle the new formation of blood-vessels is wanting.

Tubercle may therefore be defined as an inflammatory new formation, a tissue arising from an inflammation, with a scanty new formation of living matter and without any new formation of blood-vessels.

Further Changes of Tubercle. In our conception, all later metamorphoses of the tubercle become easily understood. So long as tubercle is a tissue, in spite of the lack of blood-vessels, it may give rise to new basis-substance; and if it has not exceeded a certain size, it then becomes fibrous or cartilaginous. This process leads to a *healing of tubercle* and to its obsolescence, while, as the residuum remains an indurated nodule, a granulation (in the sense of Bayle), a papillary vegetation. My views regarding the curability of miliary tubercle fully coincide with those of Empis and Waldenburg.

Far more frequently a *shrinkage of the bioplasson*, an absorption of the liquid, a so-called *cheesy degeneration* occurs, which is

due to the lack of blood-vessels, therefore to an insufficient supply of nourishing material. In this condition the infiltration may persist as a tissue for quite a time. It is only after the shriveled, and in part fatty, elements are disconnected from the mother-tissue, and from each other, that the crumbly and friable mass becomes a foreign body, like pus. It then is subject either to being encysted or to softening, to liquefaction from without, and to necrosis. The first process is the result of an inflammation of the surrounding vascularized tissue, leading principally to a new formation of callosities; the second process is due to an inflammation of the surrounding tissue, leading mainly to an exudation and suppuration. In consequence of the suppuration at the inner surface of the inflamed capsule serous pus arises, mingled with crumbs, and a cavity filled with pus—an abscess—is formed. The softened mass may become innocuous by a process of fatty and calcareous metamorphosis, and, as such, will not excite a new inflammation.

The "caseous metamorphosis" of Virchow, therefore, is due to a shrinkage, a desiccation of the new formation, which is inflammatory in the tubercle, in consequence of the absence of nourishing blood-vessels. The softening of the "cheese," on the contrary, as has been already maintained by Lombard and Andral, is invariably due to a hyperæmia or inflammation of the vascularized neighboring tissue, and to a stagnation in its blood-vessels, which is frequently accompanied by hæmorrhages and followed by the formation of pigment. *In this manner, the tubercle is removed from the group of the lymphomatous new formations and the tubercular product deprived of all specificity.*

Comparison with Suppuration. It only remains to draw the parallels between tuberculization and suppuration, as these processes are evidently kindred to each other. Reinhardt, who considered the tubercle as an inflammatory product, arising from an exudate (1847), declared the yellow tuberculous matter to be metamorphosed pus. This conception has nothing in common with our ideas. That pus may become "cheesy," in consequence of an absorption of its liquid portions, and that pus-corpuscles under these circumstances may be transformed into tubercle corpuscles,—a process which Andral has termed tuberculization of pus,—is unreservedly admitted. But this does not by any means prove that suppuration and tuberculization are identical processes. In suppuration there is also a stage in which the diseased tissue,

though infiltrated with pus, is still a tissue. The comparison with pyæmic infarctions of the lung, as alluded to before, proves this statement to be correct. The differences, however, are sharply defined. The firm, brittle, half-dry tuberculous infiltration grows gradually,—*i. e.*, in peripheral recurrences, therefore in a chronic manner,—and may remain for months in the tissue stage before it becomes softened and disintegrated. In suppuration, on the contrary, the whole process runs an acute course, being limited to a few days. Eight days after an injury which was immediately followed by purulent phlebitis, numerous suppurating pyæmic infarctions or abscesses may be found in the lungs, and the more recent infarctions appear as soft, moist, yellow infiltrations. In the production of pus within the inflammatory district, the new formation of blood and blood-vessels is likewise absent, and the living matter of older blood-vessels breaks down into the inflammatory new formation. Nevertheless, the result is strikingly different from tuberculosis.

I recall the purple inflammatory area at the boundary and the dark red hepatization in the vicinity of an infarction of the lung, before alluded to. Such an inflammatory area is constantly present around every acute abscess. The tissue in purulent infiltration is evidently richly supplied with liquid—*i. e.*, an exudation from without. When the separation of the elements follows, they are suspended in a comparatively large amount of liquid, the serum of pus. Then the result is the same as in the softening and suppuration in the formation of tubercle, namely, an abscess, though in the latter instance this result only is reached by slow process. *The abscess in the former instance is "acute," containing thick, genuine pus—the "good, laudable, and healthy pus" of the surgeons; in the latter instance it is "chronic," "scrofulous," inclosing serous pus mingled with tuberculous matter. In the former case the process is accomplished within a few days; in the latter it is extended over months and years.*

By inspissation of genuine pus and the shrinkage of the pus-corpuscles the same condition will result as after incapsulation of a softened tuberculous focus—viz.: a fatty, viscid paste, a cement-like mass, a calcareous concretion. Such a termination of suppuration is well known, especially in peripsoitic abscesses. If, on the contrary, an inundation of the inspissated pus takes place by exudation from without, in consequence of new inflammation, we find pus with "cheesy" crumbs, which is not materi-

ally different from tuberculous pus. The course and the termination may be identical with that of an acute abscess after the softened tubercle has become encysted.

Tuberculous and Scrofulous Diathesis. In conclusion, I wish to make a few remarks on the *scrofulous diathesis of the tissues.* This, according to Virchow, consists in a "feeble resistance on the part of tissues against disturbances, and a lowered capacity for equalizing disturbances; in an increased vulnerability of the parts, with a greater persistence of the disturbances." The latter conditions are the consequence of a certain "pathological constitution," which consists in a "weakness of single parts or regions and an especial weakness in their lymphatic organs," and we must understand by this "a certain incompleteness in the arrangement of the glands." Here we have the results of exact cellular-pathological research, and these results show what an important advance the cellular theory of tissue diathesis involves, in comparison with the old humoral theory of the blood krases.

The swelling of the gland is originally of an irritative, inflammatory, and hyperplastic nature; but under the influence of a certain "incompleteness in the arrangement of the glands," of a certain "diathesis," it undergoes further regressive metamorphoses, and among these the "cheesy" is the most common. According to Virchow, the same holds good for the heteroplastic new formation of tubercle proper.

In opposition to these assertions, it seems to be of advantage not to abandon the ground furnished by the above enumerated facts.

Let us say: in the inflammatory new formation, which is the *substratum,* not only of scrofulosis of the lymph-ganglia, but also of tubercle, the old blood-vessels perish in the production of a new tissue, and no new formation of blood-vessels takes place. The succeeding step will be the shrinkage of the living matter, under certain circumstances the softening of the same, etc.

Let us say, further: certain organisms have not the capacity for producing in a morbid condition, especially in the inflammatory process, abundant living matter, and we have before us the "scrofulous and tuberculous diathesis." But we do not need such a thing as a "diathesis," for we only maintain what direct observation proves. The scanty production of living matter first causes a deficiency in the new formation of blood and blood-vessels; this influences the shrinkage of the inflammatory product; this in turn causes the disintegration, and finally the softening

by inflammation of the surrounding tissue, etc. Then the circle is rounded, and scrofulosis and tuberculosis are identical, according to the ideas of Laënnec and Rokitansky.

Why, in certain organisms, are the tissues so easily inflamed? Virchow says: "It is remarkable that the disposition for tuberculosis is always associated with a disposition for inflammation." Here again a factor, the "disposition" is introduced, which ought to explain so much, and in reality does explain nothing.

Let us say: we do not know why inflammatory processes occur, with much frequency, in certain organisms. Let us further acknowledge that we do not know why inflammation ever arises spontaneously; in saying this, we speak the simple truth.

Then we are at liberty to analyze critically all experiments which have been committed, since Villemin's time, for the purpose of artificially producing tuberculosis in animals by inoculation and infection; but what would we gain? It would be folly to fight against observers—not to use a harsher expression—who, even in our day, insist upon the infectiousness of cheese, and assert that not every kind of cheese is equally infectious. Waldenburg, one of the soundest experimenters, came to the conclusion that tuberculosis, by which he, in agreement with Virchow, obviously refers only to miliary tuberculosis, is due to the taking into the circulation finely distributed corpuscular elements. These, according to his view, would be deposited in numerous scattered foci in various organs, with the formation of nodules. Inspissated, cheesy pus, and caseous tissue of the lymph-ganglia, he says, are most generally the subjects of absorption. With him, too, miliary tuberculosis is a disease of absorption, for he agrees with the idea of Buhl, that miliary tuberculosis depends upon preëxisting cheesy foci—in the face of the fact that Buhl himself admitted that in ten per cent. of the cases of miliary tuberculosis, he was unable to discover any cheesy foci whatever.

What is the real gain from all this? Many experimenters have succeeded in inducing an inflammation, every one in his own way, perhaps through embolism, perhaps by a different process. All of them have produced "miliary tubercles,"—that is, circumscribed inflammatory products in circumscribed inflammatory foci,—and it may be admitted that all this was brought about by embolism. The inflammatory products, however, did not proceed to vascularization, but shriveled up and became "cheesy," therefore tuberculous. This was not due to the skill of the experimenters, for the reason that the cause of such a result lay in the

organisms which were used for the experiment. That such a metamorphosis is easily produced in rabbits and guinea-pigs is a fact which has been well known for a long time.

I abstain from drawing conclusions concerning the therapy of tubercle. For in the question of tubercle it is doubtless Virchow's greatest merit that he has accurately defined the aims of therapy, namely: "the removal of the disposition and the avoidance of all obnoxious irritation."

To my assertions made in 1874 I have but little to add. Since that time I have examined with the microscope a large number of different organs affected with tuberculosis, and have no alteration to make in my previous statements. More than this, I have become acquainted with the anatomical features characteristic of tuberculosis, recognizable not only in single pus-corpuscles, but, from the peculiar aspect of the colorless blood-corpuscles, in every fresh drop of blood. (See page 58.)

There is a want of living matter, and to this deficiency can be traced all the features observed in scrofulous and tuberculous individuals. This involves the peculiarity that such persons are easily attacked by inflammation in general, and especially by "catarrhal" inflammation of the mucous membranes. This includes also an incapacity for reproducing blood-vessels destroyed in the inflammatory new formation of medullary elements. Blood-vessels being at first solid, bulky cords of bioplasson, which in a latter stage are hollowed out, cannot be reproduced in certain inflamed districts, and by this fact a clear understanding of the puzzle termed tuberculosis is made evident to our minds. Dyscrasia, diathesis, disposition, and kindred expressions, filling medical literature and representing medical wisdom, deserve to be abandoned. For we have something positive, something that every one can comprehend; we have facts replacing all former vague ideas expressed by a fanciful nomenclature.

Scrofulosis and tuberculosis are constitutional diseases. Want of living matter causes these and many kindred diseases, as, f. i., caries of the bones, lupus, etc. Unfortunately, I have not yet learned how to improve a person's constitution, how to increase his living matter. Could we but do that, we might also extinguish forever the misery produced by these constitutional diseases which sweep away thousands of victims. Generations are sacrificed to an irrational mode of living, to an irrational waste of living matter, in excesses of all kinds.

As to more recent researches, I merely allude to the modern views, which decidedly favor the parasitic origin of tuberculosis. This, it is said, is a contagious, an infectious disease, depending on the presence of a certain inoculable parasite. One claims that a certain disposition is required for the reception of the parasite; another says that every one of us is tuberculous, only in some there is no manifestation of the disease, etc. Tuberculosis seems a regular witches' caldron for the brewing of absurd theories.

A simple wound is sufficient to render a rabbit, a guinea-pig, a dog, etc., tuberculous, if these animals are kept in cellars, in cages, and poorly fed. Even a lion will die of tuberculosis under these circumstances. On the contrary, none of these animals will ever become tuberculous if left in freedom, and simply allowed to enjoy fresh air, proper food, and to live in a climate suitable for their organizations.

XIII.

TUMORS.*

DEFINITION. Tumors are morbid outgrowths of living tissues. An exact definition is impossible; and Virchow† himself has said: "If we were to torture a person to the last degree of endurance, he would still be unable to tell what tumors really are." The same author extends the limits of these formations to such a degree that he speaks of "tumors of extravasation and of retention"—that is, tumors which have arisen from a collection of extravasated blood, or an exudate, or physiological secretions. He furthermore dwells upon "granulation tumors," which, in the present view, are considered products of inflammation. We shall confine the idea of tumors to those formations only which, by pathologists, are termed "neoplasma" or "pseudoplasma," which originate without marked inflammatory symptoms, and terminate without a typical end; while the inflammatory process is completed by the production of a cicatrix. The best definition is undoubtedly that of A. Lücke, who says: "*A tumor is a growth produced by new formation of tissue, without a physiological termination.*"

* This chapter aims to present the outlines of oncology only. Since the establishment of my laboratory in New-York, over seven years ago, I have been generously supplied with specimens of tumors by a large number of physicians. I desire to return my thanks to them, and must specially mention by name Dr. H. B. Sands, for his kindness in this and other respects in support of my laboratory.

† "Die krankhaften Geschwülste." Berlin, 1863-67. The most exhaustive treaty on tumors, but unfortunately not completed.

Origin. All tumors originate from indifferent or medullary elements, in nearly the same manner as that by which physiological tissues are produced. No tissue can increase or pass into another, except through the intervening stage of medullary tissue, and no tumor arises from a normal tissue without the latter first passing through the same intervening stage. Virchow maintained that the new formation of a tissue—the hyperplasia—is either homologous (homœo-plastic, Lobstein) or heterologous (heteroplastic, Lobstein); the former meaning a new formation of a tissue, identical or similar to the parent-tissue; the latter a tissue differing in type from the parent-tissue. This idea cannot be carried out, as every new formation is at first heterologous—*i. e.*, medullary tissue.

The reason why a tissue sometimes produces a tumor is not understood. This, at least in some instances, appears to be due to a long continued irritation, or to an injury. But in many instances no such cause can be traced; neither are we able to explain why the reaction following irritation is, in some individuals, an acute or chronic inflammation only, and in others the production of a tumor in addition.

Tumors are tissues which, so long as they are in connection with the living organism, are living themselves—*i. e.*, pervaded by a delicate reticulum of living matter in the same manner as physiological tissues. The type of a tumor is usually that of a physiological tissue; in other words, there is no tissue constituting a tumor which differs materially from the normal tissues. A difference, however, in many instances, is established, for the reason that the tissue of a tumor remains in an embryonal or medullary condition, without passing on to a more fully developed type,—f. i., in myeloma,—or else the combination of the tissues is different from that which we know to be a physiological type—f. i., in cancer.

It is an easy matter to explain the cause of the formation of a tumor by the terms "*general diathesis*," or "*general or local disposition.*" Is there anything satisfactory in such an assumption? Is it not more correct to honestly admit that we do not know the real etiology of a tumor?

An apparent progress was made by Thiersch (1865) and by Waldeyer (1868), who claimed that the epithelia of cancer arise invariably from genuine preëxisting epithelia, and that, therefore, cancer can originate only in tissues which are offspring of the upper and under germinal layer, and in a physiological condition are constructed of epithelia. These assertions in turn have been disproved by both clinical and microscopical observation. A tumor once formed may gradually involve its neighborhood and grow at the

expense of the surrounding tissue; it then bears the name of a malignant tumor. We do not know where this capacity for infecting is located. Malignant tumors have the property of producing their own kind in internal organs, mostly in the lungs and the liver, although often their origin was far from these organs. The inference is that particles of the tumor are carried as emboli by the vascular system of these organs, and being fixed there, owing to the narrow capillaries, increase and involve the tissue in which they are lodged. Cohnheim and Maas * have attempted experimentally to prove the presence of embolisms by transferring pieces, freshly cut from the periosteum of a dog, into the jugular vein of the same animal. Between the tenth and sixteenth day after the experiment they found thĕ periosteal pieces embolized in the lungs, and exhibiting all the features characteristic of a new formation of bone-tissue. In animals which were killed after the twentieth day they found the pieces of periosteum shriveled, and no trace of ossification or of a neighboring inflammation. The above-named observers claim that their experiments prove the possibility of proliferation of cancer emboli, and, as they were not successful with scraps of periosteum, they concluded that individuals with generalized tumors lack the capacity of removing useless material from the organism.

S. Stricker † analyzes these results, and gives the following summary: (a) *Question:* Are emboli of tumors capable of growing into tumors? (b) *Experiment:* Emboli of periosteum have perished. (c) *Conclusion:* Emboli of tumors, therefore, do not perish.

Repeated experiments have been made to infect dogs, by transferring particles of freshly extirpated malignant tumors of man, by inoculation, or by injection into the vascular system. C. O. Weber and B. v. Langenbeck have reported positive results. But as these results are so few in comparison with the failures of many other experimenters, and, in addition to this, dogs are known to be frequently subject to malignant growths, the conclusions derived from such experiments must be received with caution.

Composition and Localization. In the composition of tumors connective tissue always enters, this structure being the carrier of blood-vessels. The character of the tumor depends greatly upon the amount of connective tissue present, its stage of development, and its combination with other varieties of tissue, such as muscles, nerves, and epithelia. There is a class of tumors which are composed entirely of connective tissue and its derivations, and exhibit a simple type of construction; by Virchow these are termed *simple histoid tumors.* Another class shows combinations of several tissues, imitating, to some extent, the structure of certain organs of the body, and Virchow proposes for their designation the name *organoid tumors.* In a third variety of tumors the structures of different organs are incompletely represented, and such growths are called by Virchow *teratoid tumors.* Lastly,

* Virchow's Archiv. Bd. lxx.

† "Vorlesungen über allg. u. exper. Pathologie." Wien, 1878.

several types of tumors may be combined into what Virchow designates *tumors of combination*. Tumors may be localized, that is, confined to the production of a single growth in the body; or, in other instances, several or a number of tumors may appear. In the latter case, all tumors may be produced by the same tissue system; or an originally solitary tumor may become multiple by what is called *infection*. Infection with the formation of multiple tumors may again be local if the tumors are near each other; or general, if the multiplication is brought about by the infection of different, usually internal, organs, distant from the original seat of the disease. In myeloma the infection is primarily carried by the blood-vessels; in cancers almost always by the lymphatic system.

Benignity and malignity. For a number of years tumors have been divided, according to their clinical features, into *benign* and *malignant*. This designation is based upon the nature of the tumors, as well as their clinical course. Nobody doubts that a tumor as such can never be altogether benign, as it always expresses a morbid condition, and tumors of a so-called benign character may produce distressing and even fatal results by pressure and tension, atropy of organs, or disturbance of their function. But it is of great importance to preserve the clinical nomenclature, so much the more from the fact that the pathological and microscopical features fully agree with the clinical observation.

Benign tumors are those which appear in most instances as single growths; if multiple, they arise in the same tissue system; for instance, many chondromata are found in the osseous system, many lipomata in the subcutaneous tissue, many fibromata in the skin. They remain local during their entire course, are not infectious, and do harm only by disfigurement, ulceration, pressure, and tension. Such tumors are either composed of simple tissues or combinations imitating the structure of the normal organs.

Malignant tumors are those which, though appearing originally as single tumors, subsequently, by local infection or by "metastasis,"—*i. e.*, transportation into other organs,—become multiple, therefore they are also called infectious tumors. Sooner or later, but invariably, they lead to general disturbances, to a breaking down of the constitution, and to a fatal termination, either by exhaustion, by hæmorrhage, or by interference with the function of important internal organs, such as lungs, liver, kidneys, etc.

Dubious tumors are those which at the outset exhibit a benign type, but spontaneously, or by improper or incomplete surgical interference, gradually assume the characteristics of malignant tumors; or, being from the first in a moderate degree malignant, gradually become infectious, and multiply both locally and in the internal organs.

The peculiar wasting of the body, the depreciation of the constitution, the so-called "dyscrasia," or "cachexia," which by former surgeons was considered as the primary cause of the formation of malignant tumors, to-day is regarded as of secondary origin. In former times, cancer was considered as the result of a certain dyscrasia; to-day, surgeons are satisfied that tumors of this kind are the results of a local or general disposition. These expressions, as a matter of course, explain nothing.

(a) Clinical and pathological features. The clinical differences between benign and malignant tumors are not distinctly marked in all cases, but the degree of malignity can usually be determined.

Pain in benign tumors is only exceptional, and if present it is due to pressure and tension, or a transient inflammation, and not lasting. Fibroma and cavernous angioma are sometimes painful; neuroma is, as a rule, painful in a high degree. Malignant tumors are from the first painful, or become so in their course; the more intense the pain the greater, as a general thing, is their malignity. Especially painful are malignant tumors growing in localities which are abundantly supplied with nerves—f. i., the socket of the eye, the parotid region, the tongue, etc.

The *boundary* in benign tumors is, in most cases, sharply defined to the sight or touch, and the tumor has a certain degree of movability, owing frequently to the presence of an ensheathing capsule. Malignant tumors usually appear as an infiltration, without sharp boundaries separating them from the neighboring tissues. It is only exceptional that a malignant tumor is sharply marked.

Growth in benign tumors, as a rule, is decidedly slower than in malignant. It takes a number of years for a fibroma to attain the size of a man's fist, while malignant tumors often reach the same size in a few months or years. Scirrhus or hard cancer is an exception; it arises frequently with an apparent diminution of the bulk of the organ invaded,—f. i., the female breast,—and during a number of years shows only a limited growth; while, on the other hand, some benign tumors (for instance, the so-called cysto-sarcoma or myxo-adenoma of the female breast) may increase with great rapidity.

The *integument* in benign tumors remains movable and pliable even after the tumor has reached considerable size. It is only after inflammation has been induced by pressure that a fixation of the skin occurs. Malignant tumors, though growing beneath the skin, very soon invade that structure and render it immovable before any considerable distension has taken place. There is an exception to this rule when an aponeurotic or serous layer intervenes between the tumor and the skin.

The *number*. Benign tumors are often single; sometimes, however, they may appear in large numbers,—f. i., fibroma, chondroma, lipoma, papilloma,—always growing from the same parent-tissue. Malignant tumors usually soon multiply, either in their immediate neighborhood, or as a secondary process in different localities, or in different systems and organs of the body. Exceptionally, very large and rapidly growing cancer and, as a rule, flat cancer (epithelioma, rodent ulcer) of the face remain single.

Ulceration. Benign tumors ulcerate only in consequence of local irritation, by friction of clothing, pressure, their own weight, etc. Vascular tumors (angioma) occasionally break open and ulcerate spontaneously. Malignant tumors (myeloma) often, cancer always, ulcerate, after having attained a certain and usually limited size, if situated on the surface of the body or in a cavity in direct connection with the surface. In organs of the large cavities of the body a partial disintegration or softening of malignant tumors may occur, as a process kindred to ulceration.

The *ulcerating surface* in benign tumors is smooth or covered with granulations, and discharges "healthy" pus; the same feature is exhibited by the ulcers of myeloma whenever such an ulceration occurs. Cancers, upon breaking open, present an irregularly deepened, often crateriform ulcer, with a rough, corroded base, lacking uniform granulation, and with jagged, abrupt borders, discharging a scanty, ichorous pus. The tissues in the neighborhood of a cancerous ulcer are invariably hard, almost cartilaginous, to the touch, this being one of the most important diagnostic features.

After *the formation of an ulcer* benign tumors may swell slightly, without, however, exhibiting any sign of more rapid growth, unless changing into a malignant type. Malignant tumors, after ulceration, invariably grow more rapidly. The same is the case after poulticing, irritation with local remedies, or injuries done through mistaken diagnosis with the trocar or lancet. The exuberant growth of ulcerating malignant tumors takes the form of irregular vegetations, advancing toward the place of the least resistance, outward, therefore in tumors of the surface of the body. Only flat cancer (rodent ulcer) penetrates from the surface into the depth of the part affected without producing vegetations.

The *lymphatic ganglia in the range of benign tumors* swell only when they are the seat of inflammation, in what is termed a consensual manner; similar swelling of the lymphatic ganglia may also occur in the earliest stages of development of myeloma and cancer. After the removal of the tumor the lymph-ganglia return to their normal condition. A real infiltration of the lymph-ganglion with its transformation into the tissue of the tumor, is exceptional in myeloma, but is the rule in cancer. Pain and fixation of the swelled lymph-ganglion are the clinical signs of its invasion by the morbid growth. This happens the more surely after ulceration has started in the original tumor.

Recurrence after extirpation is exceptional with benign tumors, though in some fibromata of the skin this occurs even after all diseased portions of the neighboring tissue have been carefully removed. Local reappearance is the rule with malignant tumors, with myeloma as well as cancer, and the recurrence usually takes place within the first two years after extirpation. The second tumor may appear either locally—*i. e.*, in the cicatrix after the operation—or in its neighborhood, indicating either that the "roots" of the disease had been left behind, or that at the time of the operation the infection

was present at some distant points not perceptible to clinical observation. Every recurrent tumor, as a rule, takes on a more malignant type than the preceding. Recurrence in internal organs after extirpation is considered to be due to the fact that the tissues were already affected with the disease at the time of the operation.

A multiplication of benign tumors never occurs in internal organs, and what was formerly considered a multiplication of chondroma, admits of a different interpretation. A multiplicity of malignant tumors, both myeloma and cancer, is often observed. Very probably this is due to a transportation of tissue particles from the tumor, either directly into the vascular system (in myeloma) or through the lymphatics and from them to the vascular system (in cancer). These particles produce emboli in places where most numerous and narrowest capillaries are found—*i. e.*, in the lungs and the liver. A satisfactory proof of the presence of such emboli has not as yet been obtained, neither do we understand why the embolized particles should infect the neighboring parts and transform the normal tissues into a formation like themselves. Such secondary tumors are sometimes present in enormous quantities, exhibiting the structure of the primary tumor. Not infrequently, however, secondary tumors, after cancer, do not show a trace of the characteristic epithelial structure of cancer, but that of myeloma.

(b) Histological Features. The examination of a tumor with the microscope is of the utmost importance, as, in many instances, it is only by an examination of this kind that a correct diagnosis of the nature of the tumor can be obtained.

In 1879 * I made the following statements:

"I fully concur with Prof. Lücke, of Strassburg, in the opinion that every practitioner should be acquainted with the minute structure of tumors. Such knowledge would enable him to give a more correct diagnosis and prognosis than is the case at present. Very often we can decide the future of the patient through microscopical examination of tumors, either after extirpation or before it, when small parts of the tumor are removed for diagnostic purposes.

"We know that there exists a series of tumors—the benign—which do not materially interfere with the health of the patient. Such tumors are either formations of connective tissue, with fully developed basis-substance in its four principal varieties—viz.: myxomatous, fibrous, cartilaginous, or osseous; myxoma, fibroma, chondroma, and osteoma. Or they may be composed of imitations of the fully developed tissues, sprung from the middle germinal layer of the embryo, such as angioma; lipoma, neuroma, myoma. Or, lastly, they may be combinations

* "The Aid which Medical Diagnosis receives from Recent Discoveries in Microscopy." Archives of Medicine, vol. i., February, 1879.

of epithelial and connective tissue, such as papilloma and adenoma.

"Another series of tumors, on the contrary,—called malignant,—have a deleterious influence upon the constitution of the patient. They grow rapidly, are painful, liable to ulceration, recur very often after extirpation, and produce secondary tumors in internal organs. For the differentiation of these growths we are greatly indebted to R. Virchow. He first cleared up the fact that some of these tumors are formations of connective tissue in its undeveloped embryonal or medullary condition, for which he used the rather unsuitable denomination 'sarcoma'; while others are combinations of epithelium and connective tissue—the so-called cancer forms. A third variety of tumors exhibits intermediate stages between these two kinds, and they represent what is termed, in a popular expression, suspicious tumors, such as myxo-, fibro-, chondro-, osteo-sarcoma, etc. These, upon their first appearance, do not impair the constitution of the patient; but gradually, or after repeated extirpations, or rather trials of extirpation, become decidedly malignant.

"The study of the minute anatomy of tumors, in its present condition, is as yet far from being satisfactory. Still, if the question should be raised, whether microscopy has advanced so far as to give a thorough decision of the benign, suspicious, or malignant nature of a tumor, the answer, doubtless, will be a hearty yes, it has.

"There are but very few points worthy of consideration as to the nature of a tumor. *The more of a basis-substance of the above description is present, the smaller, therefore, the amount of free bioplasson bodies, the surer it is that the new growth is of a benign nature. On the contrary, the smaller the amount of basis-substance, the larger the relative number of bioplasson bodies, the more certainly does the tumor belong to a malignant type.* The very worst tumors—glio-sarcoma, round-cell-sarcoma, and medullary cancer—exhibit a trifling amount of fibrous connective tissue. The difference mentioned, namely, is true, not only for sarcoma, but also for cancer. The more the connective tissue prevails, in comparison with the epithelial formations, the less malignant is its course, the more we are entitled to term it a 'scirrhus'; while in the fast-growing and rapidly killing medullary cancers, the frame of connective tissue bearing the blood-vessels is very small, and the epithelia are ill-developed—viz.: remain in their medullary or embryonal condition.

"Combinations of fully developed basis-substance, with partial retention of the embryonal character, are by no means rare; they involve what is termed the suspicious nature of the tumor. These tumors allow of a prognosis of recurrence after extirpation, or of a gradual change for the worse, when the surgeon, judging from the appearances to the naked eye, has not the slightest idea of the threatening danger. The inflammatory process in even benign tumors may mislead the microscopist in exceptional instances, and it is only by a thorough examination of different parts of a tumor that a correct decision as to its nature can be obtained. The presence of inflammatory elements within the connective-tissue frame of cancer is well known to be decisive of its malignant nature, and the circumstance that such elements are often found on the surface of an extirpated cancer-tumor indicates, on the one hand, that recurrence will rapidly ensue, on the other hand, that such elements play an important part in the new growth of epithelia, characteristic of cancer."

Secondary Changes. The tissues of tumors are subject to the same pathological changes which we observe in physiological tissues. These changes sometimes deprive a malignant tumor of its malignity, either in part or altogether, and they may occasionally result in a spontaneous cure of either benign or malignant tumors.

Inflammation ensues spontaneously, and after irritation or mechanical injuries from without. The inflammatory process is different here in its results, though not in its aspect, from the rapid new formation of tissue in malignant tumors. It sometimes leads to a formation of an abscess in the depth of the tumor, and may terminate, as in physiological tissues, in the production of a cicatrix. It sometimes causes ulceration—*i. e.*, a slow necrosis of the superficial layers—or gangrene, with a partial or complete destruction of the tumor. Gangrene may ensue from the weight of a pedunculated tumor, from pressure, traction, etc.

Hæmorrhage occurs most frequently in tumors which are abundantly supplied with blood-vessels, or where the blood-vessels are dilated. It may lead to the formation of encysted extravasations in the middle of the tumor,—the so-called blood-cysts,—from the walls of which again a new growth of the tissue of the tumor may arise. Hæmorrhage often causes pigmentation of the tumors. Gangrene is sometimes produced after hæmorrhage by complete destruction of the tissue, and in this way a cure may follow.

Fatty degeneration is often met with, especially in malignant tumors, and, if a larger portion be invaded, results in the formation of the "reticulum" of older pathologists. Fatty degeneration rarely appears throughout the entire tumor, but if this happens, subsequent *calcification* and *ossification* ensue, rendering the growth harmless. *Cheesy metamorphosis* is sometimes observed with the production of a yellow, friable, half-dry, shriveled mass, as seen in tubercle; this process is, as a rule, limited, and has no influence upon the further growth of the tumor.

Mucous and colloid degeneration is a rather common occurrence, especially in adenoma and cancer, and results in the formation of *cysts*. Upon this metamorphosis rests the formation of colloid and cystic cancer, and that of cysts in general. These will be dwelt upon later. *Waxy degeneration* is not infrequently found. All these metamorphoses lessen in a great degree the malignity of a tumor.

Hyaline or hyaloid degeneration results in the transformation of the tissue elements into a transparent mass, extremely indifferent to the action of acids and alkalies, and is of rare occurrence; it invades the tumor partially only and has no influence upon its general growth. The enlarged and concentrically striated elements of the tumor sometimes exhibit peculiar sprouts and pedunculated formations—the "gems" of Rokitansky and the "physalids" of Virchow. The intimate nature of these processes is far from being understood.

Calcareous deposition is observed in fatty masses, transforming them into a dry, brittle, cement-like substance; or it produces an incrustation of waxy or hyaloid corpuscles—for instance, in the psammoma; or it invades all epithelia of cancer simultaneously, rendering the tumor innocuous. Large masses of connective tissue may become calcified, especially in fibrous tumors grown from the periosteum. *Ossification*, with the production of more or less irregular systems of lamellæ, containing central medullary spaces and well-defined bone-corpuscles, occurs in a limited number of tumors—fibroma, chondroma, myeloma, and so-called osseous cancer. In most instances this process represents an only incomplete mode of healing.

Classification. For over seven years I have taught in my laboratory a systematic division of tumors—given in outlines in my essay, published in 1879, above quoted. If we bear in mind that an exact definition and classification is impossible—that there are innumerable transitions of one kind of tumor into

another, my mode of division will be found the simplest and most satisfactory, so far as my experience, which is based upon the examination of many hundred tumors, permits a definite conclusion. The system is strictly histological.

According to the four main varieties of basis-substance of connective tissue—the myxomatous, fibrous, chondrogenous, and osseous—I arrange the benign connective-tissue tumors proper as follows:

1. *Myxoma.*
2. *Fibroma.*
3. *Chondroma.*
4. *Osteoma.*

The embryonal or medullary condition of the connective tissue furnishes the well-known malignant type of:

5. *Myeloma (sarcoma).*

The combination of connective tissue with fat, with a large amount of blood-vessels, with muscles and nerves, provides four other benign varieties:

6. *Lipoma.*
7. *Angioma.*
8. *Myoma.*
9. *Neuroma.*

Any one of the eight benign types may be combined with the type of myeloma, and then they are termed: myxo-, fibro-, chondro-, osteo-, lipo-, angio-, myo-, neuro-myeloma. This combination shows that the tumor tends toward malignity.

The combination of connective with epithelial tissue results in the production of two varieties of benign tumors, in which the epithelium furnishes either the outer investment or produces glandular formations:

10. *Papilloma.*
11. *Adenoma.*

The great majority of *cysts* are secondary formations of adenoma, and may, therefore, be considered under the head of adenoma. Adenoma may be constructed of myxomatous or fibrous connective tissue: Myxo- and fibro-adenoma; or it may be built up by connective tissue in a medullary condition: Adeno-myeloma.

The combination of connective tissue with epithelia not forming glands, but either having the appearance of pegs, nests, or plexuses, or filling alveoli, surrounded by connective tissue, gives the malignant type of:

12. *Carcinoma.*

This simple division and nomenclature, as a matter of course, admits of many subdivisions and combinations. All secondary changes, however, must be separated from the primary forms of tumors, as enumerated in the above system.

1. Myxoma. Mucoid Tumor.

Myxoma or mucoid tumor is a soft, jelly-like, half-transparent growth, either sessile or pedunculated, composed of myxomatous connective tissue. Blood-vessels are sometimes abundant, at other times the supply is scanty. Myxoma may combine with other varieties of connective tissue; frequently, also, it accompanies glandular new formation.

According to the different varieties of myxomatous tissue (see page 147), myxoma appears in the following forms:

(a) Myxoma of Reticular Structure. This is composed of a delicate fibrous reticulum, holding chiefly at its points of intersection nucleus-like oblong plastids. In the meshes of the net-work there is a gelatinous, apparently homogeneous, basis-substance, which, upon being stained with chloride of gold, exhibits a delicate bioplasson reticulum. In the centers of the spaces lie single, double, or multiple plastids, some of which are about the size of a nucleus, while others show a finely granular zone of bioplasson around the nucleus. All plastids are connected by means of delicate filaments with the bioplasson contained in the basis-substance. (See Fig. 181.)

This variety of myxoma is sometimes scantily, sometimes freely, supplied with blood-vessels. In the latter case the vessels, though they have the character of capillaries, are very broad and lined with large endothelia, and in their neighborhood the reticulum is always narrower and richer in plastids than is the rest of the tissue. It is this variety which is often combined with glandular new formations of both the acinous and tubular varieties, and then produces, if pediculated, the so-called polypoid tumors of the mucous membranes. (See article "Adenoma.") Plastids crowding the meshes of the reticulum are found either in rapidly growing or in recurrent tumors, which are gradually assuming the malignant type of myxo-myeloma.

Myxomata of reticular structure are observed in the skin as flat, sessile, or pediculated, smooth or raspberry-like tumors, or they may be corrugated or lobate, and are often highly vascular-

ized. In the latter case they bear the name *myxo-angioma*. If the covering epithelium is freely supplied with pigment, it establishes the variety called *pigmented nævus;* such tumors may be congenital or they arise in middle life. Sometimes the myxomatous tissue in this situation is combined with fat, forming *myxo-lipoma*.

In mucous membranes myxoma is also common, usually as pediculated, translucent tumors in the mucosa of the nasal, the pharyngeal cavity, the gums, the larynx, the rectum, and the uterus. Often they are combined with glandular new formation, representing the variety termed *myxo-adenoma*. In the external auditory canal and the tympanum they sometimes have the

FIG. 181.—MYXOMA. PHARYNGEAL POLYPUS.

R, delicate fibrous reticulum with nuclei at the points of intersection, inclosing spaces which contain a jelly-like basis-substance and plastids; *P*, either nucleated or of the aspect of nuclei. *V*, blood-vessel. Magnified 600 diameters.

appearance of simple granulations, as observed in wounds healing by suppuration; and as both granulations and myxomata are identical in their minute structure, a positive statement as to their etiology is impossible.

Myxoma also appears along nerves, and many of the tumors termed "neuromata" are myxomatous growths arising from the

connective-tissue sheath of the nerve. Myxomatous tumors are sometimes found in the parotid gland, in the female breast, in the ovaries and the testes. In the last-named positions they may be combined with glandular and secondary cystic formations. Virchow observed myxoma in the medullary space of shaft-bones. I have seen an *intra-ocular myxoma* completely filling the slightly enlarged eyeball.

(b) Myxoma of the Structure of the Umbilical Cord. This is composed of comparatively thick bioplasson strings which, holding a varying number of nuclei, are united in a reticulum. The meshes contain the jelly-like basis-substance, and in this are imbedded apparently isolated plastids, such as are found in the tissue of the umbilical cord. The homogeneous basis-substance is sometimes mixed with fibrous connective tissue, either in single

FIG. 182.—MYXOMA OF THE PAROTID GLAND.

C, bioplasson-cords, with numerous nuclei, branching and uniting; *B*, jelly-like basis-substance, which holds single mostly central plastids, *I*. Magnified 600 diameters.

fibrillæ or in delicate bundles. Gold staining brings to view the reticular bioplasson structure within both varieties of basis-substance, as it does in the tissue of the umbilical cord. (See Fig. 182.)

The myxoma of umbilical cord-structure is rarer than the

reticular variety; it is often combined with the latter or with fibroma and chondroma. It has no blood-vessels; but these are found in the adjacent fibrous or reticular structure, never very abundantly.

(c) Myxoma of the Structure of the Thyroid Body, so called Lymph-adenoma. We may class these growths among the myxomata, on account of the presence of lymph-corpuscles, filling closed spaces or alveoli, which are surrounded by well-developed fibrous connective tissue, carrying, as a rule, numerous blood-vessels. These tumors are imitations of the structure of the thyroid body, and are benign; while tumors which are con-

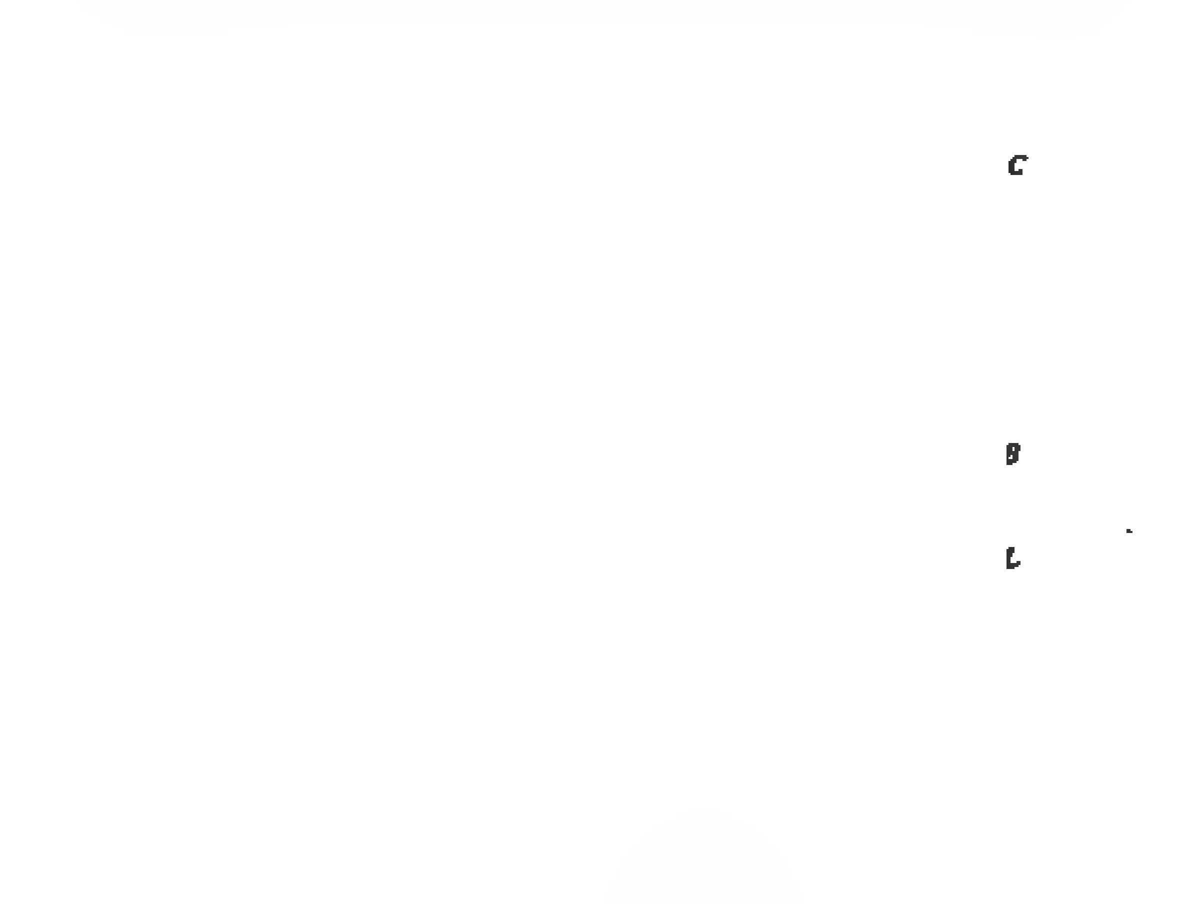


FIG. 183.—MYXOMA OR LYMPH-ADENOMA, FROM THE UPPER JAW OF A WOMAN.

C, frame of fibrous connective tissue, carrying blood-vessels, *B*; *L*, lymph-corpuscles filling the alveoli, some of which are emptied by the cutting procedure. Magnified 500 diameters.

structed on the plan of lymph-ganglia are decidedly malignant. The latter I class among the myxo-myeloma.

Tumors of the lymphomatous kind have been termed *lymph-adenoma;* but as the word "adenoma" means a glandular, therefore epithelial, structure, of which there is no trace either in lymph-ganglia or in the more fully developed alveolar structure

under consideration, the term *lymphoma* seems to be more appropriate, although this has been previously disposed of for the designation of the very malignant so-called "small cellular sarcoma."

Tumors of the structure of the thyroid body are rare, and, so far as I have been able to ascertain their clinical history, of a thoroughly benign nature. Several of the cases which have come under my observation occurred in the lateral region of the neck, independently of the thyroid body. In one case, a tumor of this kind, the size of a man's fist, occupied the region of both upper jaws, having evidently started from the lining membrane of one Antrum Highmori. (See Fig. 183.)

2. Fibroma. Fibrous Tumor.

Fibroma is a firm, dense, and opaque growth, either sessile or pedunculated, composed entirely of bundles of a dense interlacing fibrous connective tissue, which contains only a few blood-vessels. We may cut the tumor at any point, and will always meet with bundles running in different directions, which are easily recognized with low powers of the microscope. (See Fig. 184.)

Fig. 184.—Fibroma of the Vagina.

LL, bundles of fibrous connective tissue, cut longitudinally, interlacing with similar bundles at right angles, *D*; *O*, bundles cut obliquely, and *F*, bundles cut transversely. Magnified 100 diameters.

With high powers we ascertain that the bundles, like those of physiological dense fibrous connective tissue, are composed of delicate spindles, closely packed together. Between the spindles we find finely granular bioplasson and plastids, mostly reduced to the size of nuclei. The light interstices between the spindles are always traversed by extremely delicate transverse filaments, which interconnect the bioplasson formations contained in the glue-yielding basis-substance. Similar filaments connect the bioplasson formations

with the spindles. An oblique section of a bundle is obviously marked by short spindles; while the transverse section of the bundle exhibits circular formations, which are surrounded by a reticulum of bioplasson or of cement-substance. Where capillary blood-vessels traverse the tissue, the spindles are seen directly connected with the endothelial wall by means of delicate filaments. (See Fig. 185.)

The *varieties* of fibroma are:

(a) Loose fibrous connective tissue, composed of delicate bundles of fibrillæ (see page 159), builds up fibrous tumors of a

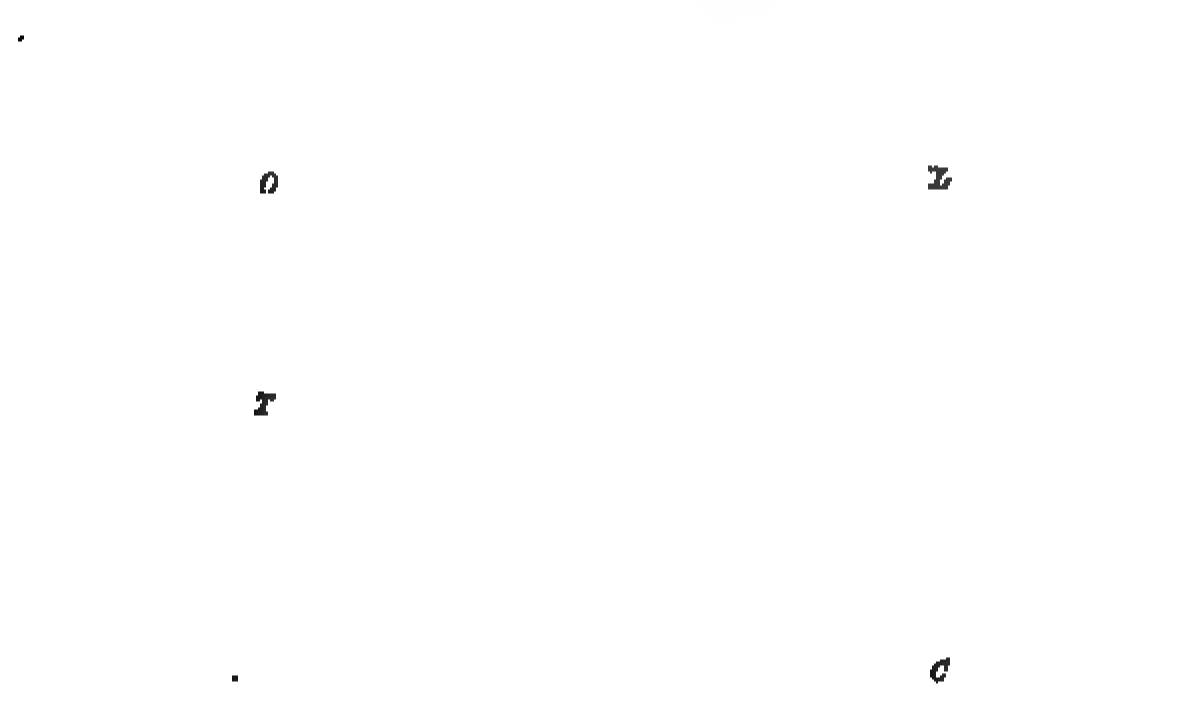


FIG. 185.—FIBROMA OF VAGINA.

L, connective-tissue fibers composed of spindles, cut longitudinally; *O*, oblique sections of spindles, *T*, transverse sections of spindles; *C*, capillary blood-vessel. Magnified 1000 diameters.

moderate degree of consistency, while the vascular supply is not abundant. They occur usually as sessile tumors of the skin, with a smooth or lobulated surface, and, if pigmented, bear the name of moles (nævus or melanoma). They are frequently found on the mucous membranes, especially of the posterior nares, the pharynx and larynx, and the uterus. Polypous, pediculated tumors of the uterus are often constructed of delicate fibrous connective tissue, which in this situation is sometimes abundantly supplied with blood-vessels. This variety blends with the next.

(b) Myxo-fibroma or soft fibroma, which may be considered as an intermediate stage between myxoma and fibroma. The myx-

omatous character is caused by the reticular arrangement of the usually delicate bundles of connective-tissue fibers, which at the same time inclose in their meshes a gelatinous, apparently homogeneous, myxomatous basis-substance, with single plastids, having the appearance of nuclei. The fibrous character is produced first by the circumstance that the reticulum is composed of a number of fibrillæ, in the midst of which delicate rod-like or spindle-shaped plastids are found, and secondly, by an interlacing of dense bundles with bundles which are loose and delicate. (See Fig. 186.)

Tumors of this kind often exhibit a transition from the myxomatous to the fibrous structure; in addition to this they

FIG. 186.—MYXO-FIBROMA, GROWN BENEATH THE SCAPULA OF A WOMAN.

Bundles of fibrous connective tissue in a reticular arrangement. The spaces contain either bundles, *O*, in an oblique or a transverse section, or a mucoid basis-substance, holding mostly central plastids, *P*. Magnified 600 diameters.

sometimes abound in fat-globules, thus assuming the character of lipoma. Myxo-fibroma is a common tumor in the skin and the mucous membranes. Bulky, folded masses of the skin, occurring in the face, on the chest, and the posterior aspect of the body, the so-called *leontiasis*, belong to this class. It is of somewhat rarer occurrence in the female breast, in internal organs, and as a periosteal growth.

(c) Dense, interlacing bundles of fibers (see page 162) are found in firm, almost cartilaginous tumors of the skin; if pediculated, they are termed *fibroma molluscum.* They develop in middle and advanced age, sometimes in large numbers all over the skin, and some of them may reach a considerable size—viz., that of a man's fist, or even that of a man's head. Tumors of this variety may be painful, like neuroma. In some individuals, especially of the colored races, there exists a peculiar liability to the formation of fibrous tumors. Around the auricles of the ear, in females, they are usually caused by the piercing for earrings. Such tumors are also remarkable for their disposition to recur after extirpation, though, as a rule, the recurrent tumors grow slowly, and retain their benign character.

(d) Scar-shaped fibroma, keloid is a flat, radiating, freely vascularized fibroma of the skin, usually painful. It grows slowly, and attracts the neighboring skin in folds. It may grow from a scar, produced by previous operations with the knife, or by caustics, or independently of any previous cicatrix. It is also characterized by an extreme proneness to recurrence. According to J. C. Warren, the cheloid is composed of more regular bundles of fibrous connective tissue than the original scar.

Combinations. Fibrous connective tissue, combined with smooth muscle-tissue, is of common occurrence in the uterus and its appendages. Sometimes smooth muscles are so abundantly prevailing in the composition of the tumor that it deserves the name of *fibro-myoma*, or *myo-fibroma.* These tumors will be considered in connection with *myoma.* Fibrous tumors, growing from the mucosa of the neck or the body of the uterus, may sometimes also exhibit an enormous new formation of tubular glands; a tumor of this construction must be considered as *adenoma.* Fibrous tumors of both the uterus and the ovaries not infrequently are supplied with a large number of blood-vessels, and then may be styled *fibro-angioma.* Sometimes fibrous tumors are the seat of partial depositions of lime-salts,—*calcified fibroma,*—and, especially those grown from the periosteum, may be partly transformed into bone—*osteo-fibroma.*

3. Chondroma. Cartilaginous Tumor.

Chondroma is a dense, firm tumor, composed of cartilage, either hyaline, fibrous, or reticular, or these varieties mixed. The fibrous portions sometimes produce trabeculæ, which carry

the blood-vessels and inclose portions of the hyaline cartilage structure.

Cartilaginous tumors are comparatively rare. They grow both from the soft tissues and from bone, and are more common in the latter situation than in the former. There are many transitions from myxomatous and fibrous into cartilaginous connective tissue, and the diagnosis often rests only on the large size and the regular arrangement of the plastids, termed cartilage corpuscles.

Chondroma is a benign tumor which may appear multiple in the same kind of tissue, but, as a rule, it does not infect the neighboring parts. In very exceptional cases, however, true chondroma attains the capacity not only to infect its neighborhood, but also to produce secondary tumors in the lungs, never surpassing, however, the size of a walnut. Virchow enumerates six cases of this kind.

Pathologists have described under the head of "chondroma" soft tumors, rich in "cells," which were imbedded in a scanty, gelatinous basis-substance. Tumors of this kind were termed *villous chondroma* and *mucous chondroma;* they may grow into the blood-vessels and produce embolic metastases. Obviously, tumors of this description, though resembling chondroma under the microscope, are not cartilaginous tumors, but either myxo-myeloma or chondro-myeloma, both being of a malignant type. If firm, genuine cartilaginous tumors are found in different localities of the body and in the lungs, also, there is no necessity for concluding that the latter are secondary formations. For the lungs hold in the walls of the bronchi enough hyaline cartilage to give rise under certain conditions (the chondromatous dyscrasia or diathesis of some writers) to primary cartilaginous tumors.

Chondroma of the "hyaline" variety is constructed like physiological "hyaline" cartilage, the difference, at least in many cases, being that in chondroma the plastids are of large size, vary greatly in shapes, and are irregularly distributed. Besides, the elements of chondroma are more coarsely granular — *i. e.*, contain more living matter than is found in normal cartilage. The gold stain reveals the reticulum in the basis-substance, just as in normal cartilage. (See Fig. 187.)

Cartilaginous new formation is found either throughout the whole tumor, or in combinations with myxomatous, fibrous, or bone-tissue; and sometimes, also, with myeloma, myoma, and cancer. The latter combinations represent Virchow's group of *teratoid tumors* — *i. e.*, undeveloped remnants of all varieties of tissues in one tumor. This condition is probably due to an undeveloped organism, being inclosed in a fully developed one — fœtus in fœtu. Formations of this kind are met with mostly in the so-called *dermoid cysts* of the ovaries and the testes, although

they have been found in other organs. I am indebted to Dr. Clinton Wagner for a specimen of an almost perfectly developed auricle of an ear, attached to the soft palate. Cartilaginous tumors grown in glandular organs not infrequently exhibit partial mucoid degeneration and secondary formation of cysts—*cysto-chondroma.* Sometimes there is a calcareous deposition in the tissue of chondroma and a combination of cartilaginous with bony tissue—*osteo-chondroma;* or, as mentioned before, a combination of chondroma with myeloma—*chondro-myeloma.* This was the condition of a tumor the size of a child's skull, grown in the testis, and from which Fig. 187 is taken.

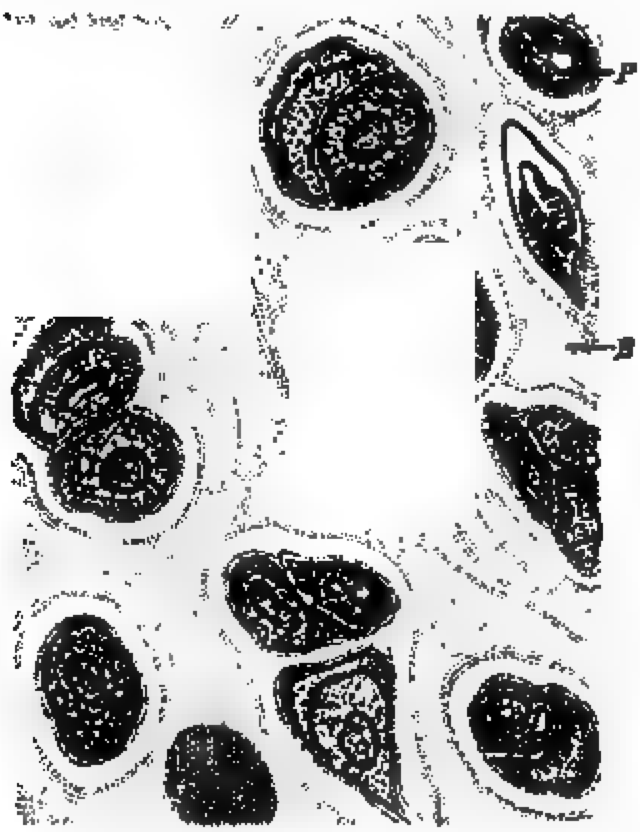


FIG. 187.—CHONDROMA OF TESTICLE.

P, plastids, mostly nucleated and coarsely granular; *B*, finely granular, so-called "hyaline" basis-substance. Magnified 600 diameters.

Among the *soft tissues,* chondroma is known to occur primarily in the parotid and the submaxillary gland, in the female breast, in the periosteum of the phalanges, in the testes, and in the lungs. It causes only local disturbances; occasionally, however, by suppuration and ulcerative destruction it may become rather serious. In *bones,* chondroma originates either from the surface (periosteum) or from the cancellous portion, the diploë of skull-bones and the central medullary space of shaft-bones. The most common places for chondroma to appear are the phalanges and metacarpal bones of the fingers, more rarely those of the toes; next, the epiphyses of the shaft-bones, the carpal and tarsal bones, the ribs, the sternum, and very rarely the pelvis and skull-bones, the upper maxillary bone, and the socket of the eye. The simultaneous growth of a number of cartilaginous tumors in several of the above enumerated localities has also been observed. What pathologists describe as central chondroma, arising from the medulla of the shaft-bones, in many instances probably was, judging from the clinical phenomena and the multiplication in the lungs, myxo- and chondro-myeloma, but not pure chondroma.

4. Osteoma. Osseous Tumor.

Osteoma is a solid tumor, composed of bone-tissue, and growing without symptoms of inflammation, in contradistinction to the exostosis or the osteophytes, which are products of osteitis and periostitis. Corresponding to the two principal varieties of bone-tissue (see page 223), we have two kinds of osteoma:

(a) Cancellous or Epiphyseal or Spongy Osteoma. This occurs on the epiphyseal ends of shaft-bones, closely connected with the cancellous portion; it is found only in youth, and is never a primary formation after the thirtieth year of life. Such tumors lie beneath the covering periosteum, and at their free surfaces

Fig. 188.—Cancellous or Epiphyseal Osteoma, from the Second Phalanx of the Thumb.

T, trabeculæ of bone-tissue, indistinctly lamellated, *M*, large and irregular medullary spaces, containing blood-vessels and medullary tissue. (The latter shriveled, owing to the circumstance that the specimen was brought for examination in a half-dry condition.) Magnified 100 diameters.

are usually lobular. They are either inclosed by a thin layer of compact bone-tissue or by a layer of hyaline cartilage. They are composed of indistinctly lamellated trabeculæ of bone, containing regularly developed bone-corpuscles, and inclosing medullary spaces, which vary greatly in size and are filled with medullary tissue and blood-vessels. (See Fig. 188.)

Formations closely allied to cancellous osteoma are the *processus supracondyloidei*, which Hyrtl first described as congenital

formations; they occur at the articular ends, mostly, of the humerus and the femur, analogous to the *processus trochleares* of some animals. To these may be added the bony formations at the points of insertion of the tendons, muscles, and aponeuroses, which Virchow termed *exostoses apophyticæ*. They are either directly connected with the bone, or take rise independently of it (so-called tendon bones). These bony structures originate, unconnected with inflammation, perhaps on account of an excess of lime-salts in the organism. Maslowsky has succeeded in producing calcareous deposition and ossification in the muscles of animals, in the vascular system of which, for a certain length of time, he had injected lactate of lime. Bony formations in the dura mater, the muscles, and the lungs are products of inflammation.

(b) Compact or eburneal osteoma is a rare tumor; it occurs on the bones of the face, the skull, the scapula, the pelvis, and the phalanges; its favorite locality is the frontal bone. It has a smooth or slightly nodulated surface, and very rarely attains any considerable size. It is composed of a more or less regularly lamellated bone-tissue, imitating in its structure the outer peripheral layer of compact bone, and is scantily supplied with medullary spaces. These, on the surface of the tumor, are, as a rule, large, and contain several blood-vessels; while the main mass shows only irregular Haversian canals, which contain one capillary blood-vessel. Toward the point of attachment the compact bone formation usually blends with the cancellous structure. (See Fig. 189.)

The cement-layer of the roots of teeth not infrequently develops into compact osteoma, which sometimes reaches a considerable bulk. Tumors of the dentine are entirely different formations; for their designation Virchow has proposed the term *odontoma*. These are composed of dentine, with irregularly arranged dentinal canaliculi, similar to formations of secondary dentine and the so-called pulp-stones. (See chapter on teeth.)

Bone-tissue is often found combined with other varieties of tumors, such as fibroma, chondroma, myeloma, and it is asserted that it also unites with cancer and forms the "malignant osteoid" of Joh. Müller. The terms employed to designate tumors of these varieties are osteo-fibroma, osteo-chondroma, and osteomyeloma. In all these instances the bone-tissue is unquestionably a secondary formation.

Psammoma is the term applied by Virchow to a class of tumors characterized by the presence of peculiar corpuscles, which usually exhibit a distinct concentric striation, or appear as nodular or rod-like masses. Virchow maintains that these tumors may be either homologous (benign) or heterologous (malignant)—*i. e.*, represent transitions into sarcoma. Virchow proposes to call the corpuscles *arenoid*—that is, sand-like; they are a normal feature in the anterior portion of the glandula pinealis, where they form the acervulus cerebri. Besides, they are met with in the cerebral and spinal dura mater, especially in the Pacchionian bodies, and in the arachnoid. They are amylaceous corpuscles, infiltrated with lime-salts, although Virchow insists upon their being different from the corpora amylacea on account of the blue stain of the latter, shown when treated with iodine. Such corpuscles were found also in enlarged hyperplastic lymph-ganglia. The tumors containing them occur both in the brain-tissue and in its investing membranes, especially the dura mater, in the optic nerve and its investments, and in the retina. (See Fig. 190.)

M

L

FIG. 189.—COMPACT OR EBURNEAL OSTEOMA, FROM THE FRONTAL BONE OF A MAN.

L, lamellated bone-tissue, pierced by medullary spaces, *M*, which toward the periphery of the tumor are large and contain several blood-vessels; while in the more central portions of the tumor the medullary spaces are reduced to irregular Haversian canals. Magnified 100 diameters.

The term "psammoma," applied to a tumor, is obviously superfluous, for the arenoid corpuscles do not determine the nature of the tumor, which may be a myxoma, a fibroma, an angioma, or a myeloma, consequently widely differing in pathological features. The arenoid corpuscles are secondary and incidental formations in these tumors. The same holds good for pigmented tumors, which occur in rare cases in the pia mater, and are termed

melanoma. The presence of pigment alone is not sufficient to characterize the nature of the tumor. There is, however, no objection to calling a tumor which contains sand-like bodies an "arenoid fibroma, angioma," etc., and a tumor which contains pigment granules a "melanotic fibroma, myeloma," etc.

5. Myeloma or Sarcoma.

The special character of this group of tumors was first determined by Virchow. He considers the structure to be connective tissue in an embryonal or medullary condition, without any epithelial elements, and thus sharply marked from cancer. All later researches have corroborated Virchow's views. We

Fig. 190.—Arenoid Myxoma (Psammoma, Virchow) of the Dura Mater.

T, trabeculæ of fibrous connective tissue, holding partly sessile, partly pediculated, arenoid corpuscles, *A*, or elongated calcareous formations, *C*. Magnified 50 diameters.

define sarcomata as Virchow defined them—that is, connective-tissue tumors, in which very little or no basis-substance is developed. We object, however, to the word "sarcoma," as this means *fleshy tumor*, and would substitute for it the old term "myeloma,"—viz., *medullary tumor*,—as this accords better with the histological features.

Virchow divided sarcomata into the following varieties: *(a) net-cell sarcoma; (b) spindle-cell sarcoma; (c) round-cell*

sarcoma; (d) giant-cell sarcoma, and *(e) melanotic sarcoma.* Billroth added another variety, the *alveolar sarcoma.* In analyzing the different varieties of myeloma, we are satisfied that there are but two principal forms, which I propose to term *(a) globo-myeloma*, corresponding to Virchow's round-cell sarcoma; and *(b) spindle-myeloma*, corresponding to Virchow's spindle-cell sarcoma. Both varieties are sometimes found in one tumor.

(A) Globo-myeloma is composed of medullary tissue, with globular elements. (See page 147.) These contain single or double nuclei, or they are divided into smaller plastids, evidently in the mode of growth and multiplication of the elements. Tumors of this kind, as a rule, are of a grayish-red or grayish-yellow color, containing a comparatively small number of blood-vessels. Its sub-varieties are:

(a) Globo-myeloma, composed of large plastids (large round-cell sarcoma). These are separated from each other, either by a narrow rim of cement-substance or by a delicate fibrous reticulum; all elements, however, are connected by means of delicate filaments. The nuclei are large, and contain several coarse granules—nucleoli. (See Fig. 191.)

FIG. 191.—GLOBO-MYELOMA, COMPOSED OF LARGE PLASTIDS. FROM THE INTERMUSCULAR TISSUE OF THE FOREARM OF A WOMAN.

The globular, slightly flattened corpuscles are separated from each other by a scanty basis- or cement-substance. C^1, solid cord, indicating a new formation or a retrogression of a blood-vessel; C^2, fully developed capillary blood-vessel. Magnified 600 diameters.

(b) Globo-myeloma, composed of small plastids (small round-cell sarcoma), the structure closely resembling the so-called adenoid or lymph-tissue. A delicate fibrous reticulum holds varying numbers of plastids, which are mostly solid, having the appearance of lymph-corpuscles, some being surrounded by a finely granular bioplasson. This form represents the "lymphoma" or "lympho-sarcoma" of authors. (See Fig. 192.)

(c) Glioma or glio-sarcoma. Virchow applies the term "glioma" to tumors arising from the connective-tissue formations

of the central nervous system and the retina, without reference to their intimate histological structure. Recently, efforts have been made to remove glioma from the group of myeloma. Clinical observation shows the extreme malignity of many of these tumors; microscopic examination shows their close relationship to myeloma, and that a varying amount of fibrous connective tissue may enter into their construction.

Glioma is composed of elements closely resembling those found in the cortex cerebri and cerebelli, and those of the granular layers of the retina. These elements exhibit comparatively large nuclei, around which is a scanty rim of granular bioplasson.

In rapidly growing tumors the elements exhibit distinct proliferation, and in many instances flatten each other. Between

S

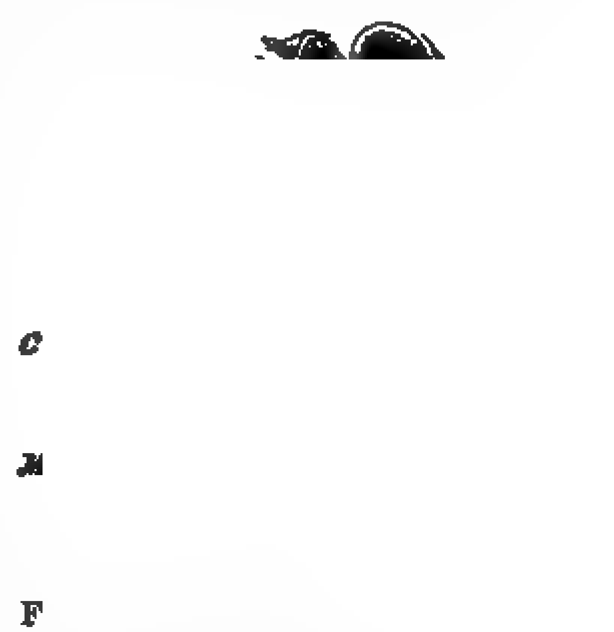
FIG. 192.—GLOBO-MYELOMA, COMPOSED OF SMALL PLASTIDS. FROM THE TESTICLE OF AN ADULT.

T, transverse section of a seminiferous tubule, toward the epididymis; *S*, myeloma of the type of lymph-tissue (adenoid tissue); *TS*, transition of the epithelia into myeloma tissue. (For high amplification of the same tumor, see Fig. 206.) Magnified 200 diameters.

them we see a delicate layer of cement-substance, traversed by the connecting filaments. In the cement-substance homogeneous plastids occur, indicating either development of glioma- or spindle-shaped elements, which latter belong to the connective-tissue frame. (See Fig. 193.)

(B) Spindle-myeloma is composed of medullary tissue with spindle-shaped elements. The difference between physiological

medullary and myelomatous tissue is that, as a rule, in the latter the bundles of the spindles are interlacing — *i. e.*, course in different directions, like interlacing fibrous connective tissue. Sometimes, however, the bundles take an almost parallel course, and can be separated into radiating groups of spindles, the *fascicular spindle-myeloma* (fascicular spindle-cell sarcoma of Virchow, fascicular cancer of older pathologists). The sub-varieties of spindle-myeloma are:



RECURRENT TUMOR AFTER THE ENUCLEATION OF THE EYEBALL FOR GLIOMA OF THE RETINA.

M, glioma element with several nuclei; *MS*, group of glioma elements, sprung from division; *GC*, fully developed glioma element, *CF*, spindle-shaped fibers between the groups of glioma elements; *E*, capillary blood-vessel. Magnified 800 diameters.

(a) Spindle-myeloma, composed of large plastids. These are separated from each other by a light rim of cement-substance or a delicate fibrous reticulum, most distinct in transverse sections of the bundles. The nuclei of the spindles, as a rule, are seen as homogeneous and shining lumps, often exhibiting marks of division and multiplication. Between the nucleated spindles there are fusiform fields, containing a finely granular or homogeneous mass; this indicates an approach to basis-substance. (See Fig. 194.)

(b) Spindle-myeloma, composed of small plastids, either interlacing or taking an exclusively parallel course. In many instances this tissue bears a close resemblance to non-medullated nerve-fibers. vidently, tumors composed of such delicate spindles are often istaken for true new formations of nerve-fibers, a neuroma. his variety of myeloma is not of infrequent occurrence in the oroid, and often contains clusters of pigment which previously longed to the choroid or to the layer of pigmented endothelium the retina. Such pigment clusters, however, unless present in arge number, will not justify a diagnosis of a melanotic myea. (See Fig. 195.)

(c) Spindle-net myeloma (net-cell sarcoma of Virchow). In variety spindles of varying sizes branch at acute angles, unite form a reticulum. The meshes of the reticulum are elongated, hold a slight amount of basis-substance and globular or

oblong plastids, which are apparently isolated. The more nearly the reticulum approaches to a circular arrangement, and the smaller its composing spindles, the more closely allied is this variety to that of myxo-myeloma. Finally, all distinguishing marks are lost, and spindle-net myeloma and myxo-myeloma blend with each other. (See Fig. 196.)

The "*giant-cell sarcoma*" of Virchow cannot be considered as a tumor *sui generis*, for the so-called "giant-cells" never constitute the entire mass of the tumor. They are intermixed with fibrous connective tissue, as well as with fibro-myeloma, and are more numerous and better developed the greater the amount of basis-substance contained in the surrounding tissue. As, in our view, the multinuclear plastids arise from a fusion of medullary elements, whenever there is a tendency to form territories, usually of cartilage and bone, it will be understood from this fact that the malignity of these tumors is very slight. Their favorite site of growth is the periosteum, especially the periosteum of the jaw-bones (so-called "epulis"), and a permanent cure will ensue if the tumor is thoroughly extirpated. I have examined several globo- and spindle-myelomata which had grown from the maxillary bones, where very little basis-substance

FIG. 194.—SPINDLE-MYELOMA, COMPOSED OF LARGE PLASTIDS. FROM THE OMENTUM OF A WOMAN.

L, nucleated spindles cut longitudinally; *O*, spindles cut obliquely; *F*, spindles cut transversely. Magnified 600 diameters.

FIG. 195.—SPINDLE-MYELOMA, COMPOSED OF SMALL PLASTIDS. FROM THE CHOROID OF AN ADULT.

L, nucleated spindles cut longitudinally; *O*, spindles cut obliquely; *P*, pigment clusters from the former pigmented endothelium of the retina. Magnified 600 diameters.

could be found; therefore, they were decidedly malignant. In tumors of this sort the multinuclear plastids were always scanty and imperfectly developed—*i. e.*, composed only of clusters of medullary corpuscles. The comparatively benign type of "epulis," however, is more common than the malignant. (See Fig. 197.)

Any myeloma, including the alveolar myeloma, may be the seat of a more or less abundant formation of pigment, and is then termed melanotic myeloma. The pigment, therefore, is merely an incidental feature of myeloma, but it is known to increase greatly the malignancy of the tumor. The origin of the pigment was

FIG. 196.—SPINDLE-NET MYELOMA, FROM THE SUBCUTANEOUS TISSUE OF THE LEG OF A MAN.

S, nucleated spindles branching and uniting; the meshes contain a finely granular myxomatous basis-substance, and *G*, apparently isolated globular or oblong plastids. Magnified 600 diameters.

formerly attributed to extravasated blood. I have ascertained that in such tumors a very profuse new formation of living matter takes place, which causes the production of numerous hæmatoblasts,—*i. e.*, solid lumps of living matter,—which in their earlier stages of formation, for reasons unknown, are supplied with the coloring matter of the blood. (See page 98.) From

these hæmatoblasts, before their development into red blood-corpuscles, arise the pigment clusters. The process can be best studied at the border of melanotic myeloma of the choroid in the region of the vitreous body. Here the hæmatoblasts originate in the middle of the vitreous body, being characterized by a globular shape, luster, distinct yellow color, and their small size, as compared with fully developed red blood-corpuscles, for which they often are taken. How far the hæmatoblasts participate in the new formation of the myeloma elements I was unable to ascertain; but unquestionably they are the source of pigment in melanotic myeloma. (See Fig. 198.)

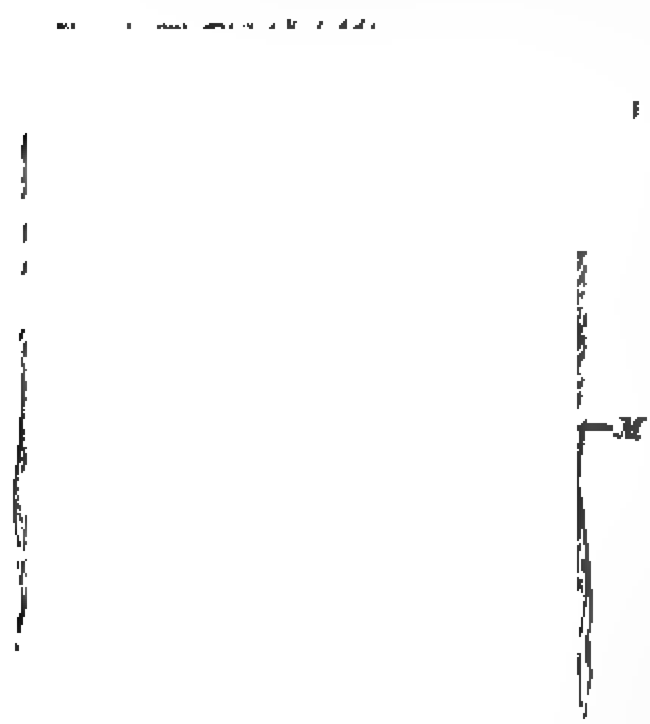


FIG. 197.—FIBRO-MYELOMA, WITH MULTINUCLEAR PLASTIDS. FROM THE LOWER JAW OF A YOUNG MAN.

M, group of medullary corpuscles approaching the stage of indifference, *G*, multinuclear plastid, so-called giant-cell. Magnified 600 diameters.

Combinations of Myeloma. Myeloma may combine with any variety of connective tissue- and epithelial tumors, which means that a portion of the tumor possesses fully developed basis-substance, while another portion has but little or lacks it entirely. A tumor with originally well-developed basis-substance may gradually change its character, and in the portions of later growth be without basis-substance. With this failure in the production of basis-substance a more rapid growth of the tumor ensues, and it assumes a more malignant type. As before mentioned, such tumors are clinically considered "dubious" in their nature, although some of them are either of a marked malignant character, or become so in a relatively short time. According to our nomenclature, the various combinations of these tumors are termed as follows:

(a) Fibro-myeloma, the "fibroplastic" tumor, or "recurrent fibroma" of older pathologists. It consists of bundles of fibrous connective tissue, between which are large numbers of usually globular elements; or the tumor originates from fibrous tissue,

f. i., the derma of the skin,—and by degrees entirely replaces it. The fibrous structure of such tumors is sometimes very faintly marked; but their comparatively slight degree of malignity is recognized by the presence of a finely granular basis-substance between the homogeneous plastids, which, of the size of nuclei, are scattered at regular intervals. Sometimes these tumors are lobate or nodular, and covered with a richly pigmented rete mucosum (mole, nævus). With advancing age or

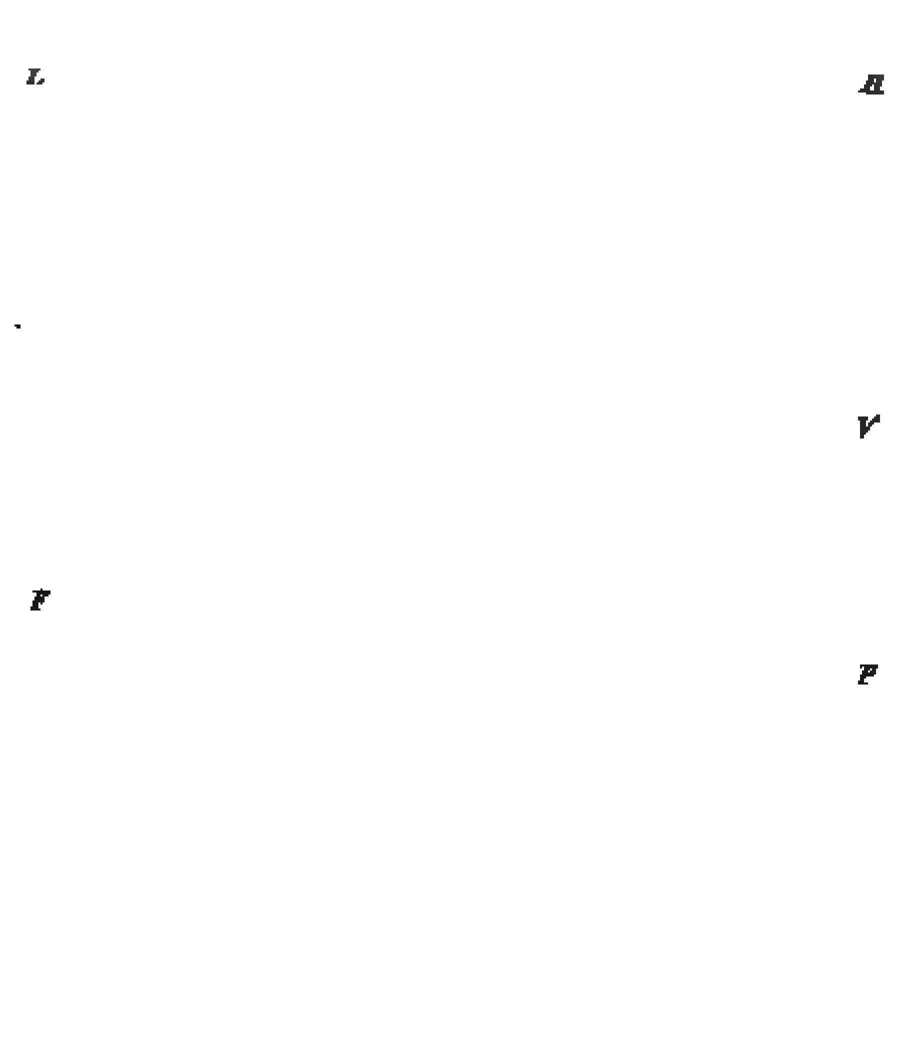


FIG. 198.—MELANOTIC GLOBO- AND SPINDLE-MYELOMA OF THE CHOROID.

L, group of globular pigmented plastids; *F*, delicate fibrous connective tissue at the periphery of the tumor; *H*, hæmatoblasts; *P*, pigment cluster; *V*, vitreous body. Magnified 600 diameters.

improper treatment they readily assume the character of malignant myeloma. (See Fig. 199.)

(b) Myxo-myeloma is constructed on the plan of myxomatous tissue—*i. e.*, a delicate fibrous reticulum contains in its meshes plastids in different stages of development; but they are far

more numerous than in simple myxomatous tissue. Myxomatous tumors, especially the so-called polypoid tumors, often exhibit some of the features of this type, indicating a rapid growth of the tumor and its liability to recur after extirpation. If the reticulum is very delicate, and the inclosed plastids very small, not exceeding in size the lymph-corpuscles, the type of a lympho-myeloma (small globo-myeloma) is established, which growth is of intense malignity. Myxo-myeloma, therefore, blends with the spindle-net myeloma, as well as with the lympho-myeloma. (See Fig. 200.)

(c) Chondro-myeloma differs from chondroma in the softness of its basis-substance, while the plastids may exhibit the size and shape of cartilage corpuscles. Many of the so-called "malignant chondromata" probably are chondro-myeloma, and I know this mistake to have been made by good pathologists. The term "chondro-myeloma" may also be applied to tumors which, in a tissue showing all the features of globo-myeloma, contain islands of well-developed cartilaginous tissue.

FIG. 199.—GLOBO-MYELOMA, WITH A MARKED FORMATION OF BASIS-SUBSTANCE. FROM THE ABDOMINAL WALL OF AN ADULT.

C, capillary blood-vessel in transverse section; *A*, artery in transverse section. Magnified 600 diameters.

FIG. 200.—MYXO-MYELOMA. RECURRENT PHARYNGEAL POLYPUS.

B, portion of myxomatous structure; *P*, portion of myelomatous structure; *V*, large capillary blood-vessel. Magnified 600 diameters.

(d) Osteo-myeloma is a term used for the designation of myelomatous tumors growing in the middle of the bone, or of

tumors in which within myeloma-tissue new formation of bone has taken place. The error resulting from such a nomenclature is not great, as in many instances it is impossible to decide whether the bone-tissue in the tumor is a remnant of the former physiological bone, or whether it is newly formed. A great irregularity in the size and the arrangement of the bone-corpuscles will favor the view of the bone being newly formed,

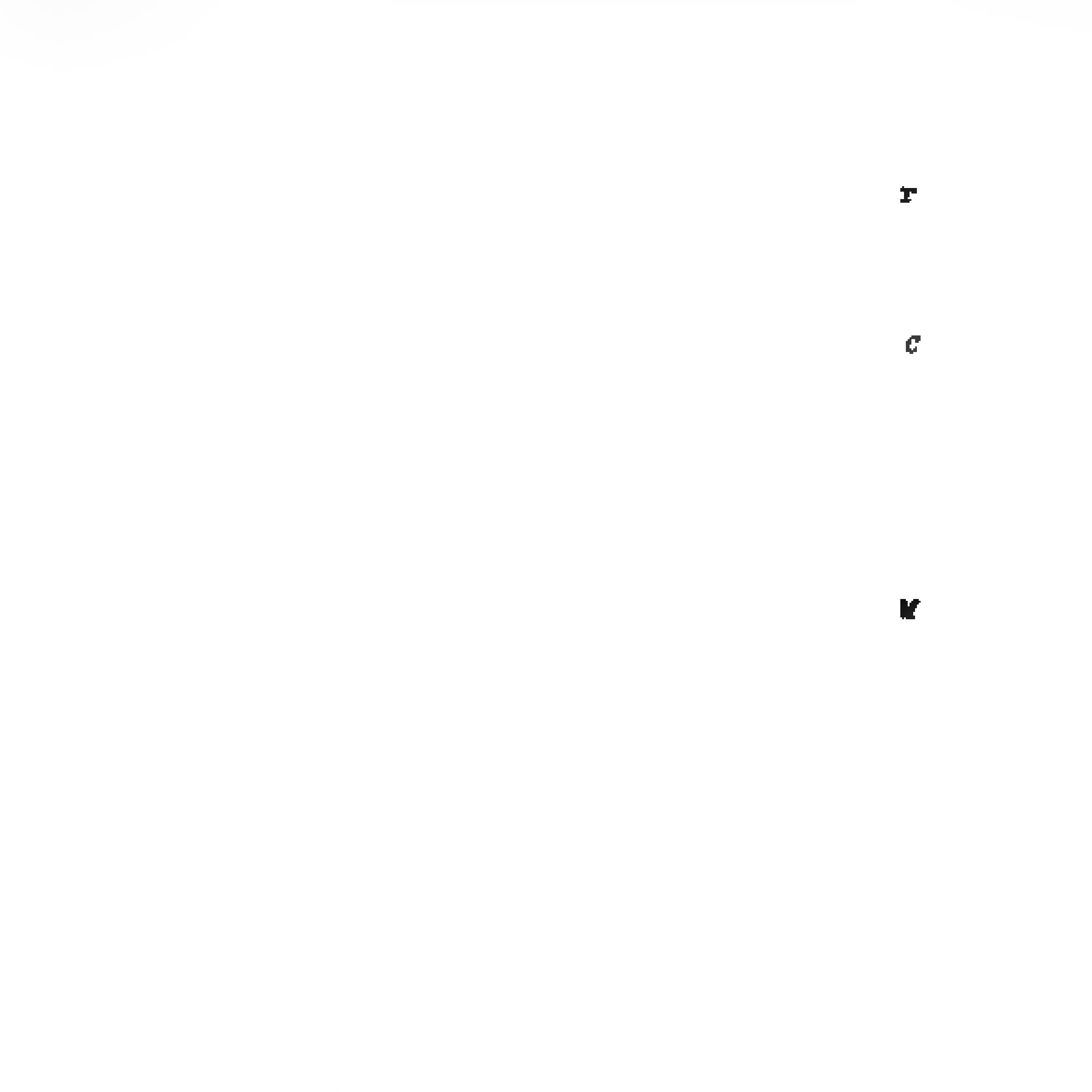


FIG. 201.—OSTEO-MYXO-MYELOMA, FROM THE HIP-BONE OF A GIRL.

T, trabeculæ of newly formed bone, with large and irregular bone-corpuscles; *M*, myxomatous tissue, changing to myeloma; *C*, plastids, infiltrated with lime-salts. Magnified 400 diameters.

and this view is strengthened if we are able to trace the new formation of bone through all its stages, from the first infiltration of plastids with lime-salts up to the appearance of trabeculæ. Besides, it is granted that the myeloma tissue (myxo- or fibro-

myeloma) is not of a very malignant type where bone-tissue is formed, though it is possible for the tumor to change to a more malignant form. Myeloma, with numerous globular or spindle-shaped elements, is, as a rule, deficient in new formation of bone. The tumor the size of a child's head, from which Fig. 201 is taken, for a number of years grew slowly, though steadily, while later it increased rapidly to a fatal termination.

The combinations of myeloma tissue with other varieties of tissue (lipoma, angioma, myoma, neuroma, and adenoma) will be considered in the articles treating of these tumors. Here I only mention that, according to Virchow, there also exists a combination of cancer with myeloma—a view which I, from a large number of observations, can corroborate.

Alveolar myeloma (Billroth) is of a dubious nature. Most pathologists regard it as cancer, but it seems more correct to class it among the myelomata; for it shows all the clinical and pathological features of such tumors—nay, it appears occasionally as a secondary tumor after primary myeloma. A delicate frame of connective tissue forms the alveoli, which are filled with globular, oblong, or irregular and usually nucleated plastids, very loosely connected with one another—so loosely, that in sections the alveoli appear incompletely filled. The plastids never reach the size and the polyhedral shape of epithelia, so characteristic of cancer; those nearest to the connective-tissue frame are pear-shaped, being attached to the frame by a slender pedicle. I have seen this variety of tumor in the groin, in the testis, the omentum, and the liver; in both the last-named positions the tumors were secondary, and that of the liver was of a pronounced melanotic type. Perhaps this tumor represents a transition of myeloma into cancer, a transition which in the opposite way—cancer to myeloma—is of more common occurrence. (See Fig. 202.)

Myeloma is a malignant tumor, and any portion of the connective tissue of the body may serve as its starting-point. In fact, this tumor has been observed in all parts and all organs of the body, except in horny tissue. Contrary to cancer, it is often a growth of childhood and youth, and may occur at any age. Its malignity is intensified when the constituent elements are small, the blood-vessels abundant, and the basis-substance scanty. The presence of pigment, both in the fibrous and medullary portions of the tumor, greatly increases its malignant character. Not infrequently local irritation, particularly injuries of all kinds, can be traced as the exciting cause of myeloma.

The clinical diagnosis, in many instances, is possible when there is a rapid growth and local multiplication; often, however, the tumor has all the appearances of a benign growth, while microscopic examination reveals its malignant nature. An error in diagnosis may occur owing to the circumstance that myeloma, upon approaching the surface, as a rule does not cause ulceration of the skin, neither are the neighboring lymphatics enlarged or painful. Sometimes myeloma appears in great numbers, almost simultaneously in different parts of the body, and tumors, which already have reached a certain size, may gradually disappear and return again. Local recurrence after extirpation is a common

FIG. 202.—ALVEOLAR MYELOMA, FROM THE MESENTERY OF A YOUNG MAN.

F, frame composed of a delicate fibrous connective tissue, carrying blood-vessels, inclosing alveoli, the latter contain *C*, the spindle-, pear-, or irregularly shaped plastids. Magnified 600 diameters.

feature; and so is multiplication, especially in the lungs, which are sometimes found crowded with whitish, slightly vascularized, tumors, the size of a poppy-seed, a hazel-nut, or a walnut. The same may be found in the pleura and the peritoneum. Melanotic myeloma selects the subcutaneous tissue, mostly of the

hands and the feet, as a point of departure, from which it gradually invades large portions of the surface of the body, in some cases so rapidly that inflammatory symptoms are observed with the formation of every new nodule. In such cases, the secondary tumors in internal organs are either white or pigmented. The patients die showing the symptoms of exhaustion (cachexia, marasmus) or of septicæmia, in consequence of extensive gangrene of the tumors. Mucous or colloid degeneration may also occur, and this change renders the tumor much less malignant.

In the growth of myeloma, muscle- and nerve-tissue are transformed into medullary tissue. If the tumor has originated in a glandular organ, the epithelia are also converted into medullary plastids, and glands are either completely destroyed or partly enlarged, and even newly formed. In the latter cases, peculiar cauliflower-like vegetations are produced within the gland, owing to the encroachment of the myeloma tissue. Under these conditions, cysts are very common occurrences—f. i., in cysto-myeloma of the female breast or the ovary.

THE CHANGES OF EPITHELIA PRODUCED BY GROWTH OF MYELOMA. BY RUDOLPH TAUSZKY, OF NEW YORK.*

It is known that myelomatous growths, which have originated either in the cutaneous or subcutaneous tissue, and also those which appear in tissues more deeply situated, as they approach the surface, sometimes produce ulcerative processes in the integument. This always becomes attenuated before the ulcerative process, often accompanied with inflammatory symptoms, begins. After a certain time a loss of substance is observed at the most prominent point of the tumor, which gradually enlarges; and at its base the tumor is seen as a reddish, slightly nodular, or even smooth mass. The ulcer produces, as a rule, a relatively small quantity of pus. Clinically, this is a valuable diagnostic symptom of myeloma. Cancer invariably gives rise to an ulcerative process in the skin, and the ulcers thus produced present uneven, nodular, and irregularly granulating surfaces, yielding pus or ichor.

The question now arises: What histological changes take place in the wasting process of the epidermis? Of course, with the customary expression of "fading or dying" of the epithelium only a clinical fact is recognized, and the cause must be sought for in anatomical changes. At the same time, the question may be answered: What changes does the epithelium of glandular organs undergo when myeloma appears in them?

The literature of the morbid growths under consideration gives no satisfactory explanation of the question. I therefore examined a number of myelo-

* Abstract from Dr. Rud. Tauszky's essay: "Ueber die durch Sarcomwucherung bedingten Veränderungen des Epithels." Sitzunsber. d. Kais. Akademie d. Wissensch. in Wien. Bd. lxxiii. The term "sarcoma" is changed into "myeloma," and that of "protoplasm" into "bioplasson."

mata of the skin and glandular organs, with special reference to the behavior of the epithelium. My specimens were: (1) A myeloma about the size of a child's fist, which was extirpated from the abdominal wall of a man fifty-five years of age; (2) myeloma growths of the size of walnuts, which appeared in the right groin of a man sixty-nine years of age, and which, after repeated extirpations, were followed by numerous secondary myeloma nodules in the lungs; (3) a myeloma of the testis of a man, aged forty-eight years, nearly the size of a child's head; (4) a myeloma of the submaxillary gland, of a man aged

FIG. 203.—FIBRO-MYELOMA FROM THE ABDOMINAL WALL OF AN ADULT.

P, papillæ, cut transversely; *D*, derma of skin, with commencing transformation into myeloma; *B*, blood-vessel, *R*, rete mucosum. Magnified 200 diameters.

seventy-two years, as large as a chicken's egg; (5) myeloma nodules from the liver of a man, aged fifty-nine, which occurred as a secondary growth after extirpation of a tumor of the eyeball, simultaneously with nodules in the omentum, the mesentery, and the walls of the small intestines. Among

these were represented the varieties called "round-cell sarcoma"; "spindle-" combined with "round-cell sarcoma" and "alveolar sarcoma."

The changes in the epithelium, which are induced by the growth of myelomatous tumors, may be divided into two groups. The first embraces the purely inflammatory process; the second includes changes that lead to the production of myeloma elements from epithelium. No distinct boundary can be drawn between these two groups; for the changes observed in inflammation are like those accompanying the growth of tumors, inasmuch as in both instances new formation of living matter and production of new elements results.

Inflammatory changes. Specimens of the tumor (1) taken from the integument near the ulceration show, with low power, that the epidermal layer was thinned in several places. (See Fig. 203.) We could see that the pigmented layer which constitutes the border nearest the connective tissue is in a condition of moderate "cell-infiltration"—that is, inflammation. The pigmented epithelium is arranged irregularly, and is deficient in many places. Higher amplification proves that the epithelium along the connective tissue is broken up into elements, which do not differ from those which originate in connective tissue; only the pigment is a reminder of their origin, but the pigment in this situation also gradually decreases as the inflammatory changes proceed toward the epithelium. We meet with dispersed pigment granules, or groups of such granules, apparently remnants of former epithelium, though the larger

P

FIG. 204.—FIBRO-MYELOMA FROM THE ABDOMINAL WALL OF AN ADULT.

D, bundles of connective tissue of derma in transformation to bioplasson, *V*, bloodvessel, P^1, transformation of pigmented epithelia into non-pigmented plastids; P^2, epithelia breaking down into pigmented lumps. Magnified 800 diameters.

mass of pigment has disappeared, perhaps by interference with the nutrition of the granules themselves, which have not yet been entirely deprived of vitality. Thus the epithelium containing pigment is changed directly into indifferent bioplasson bodies, from which, in turn, new elements arise. A real new formation has as yet not taken place, but out of specific elements indifferent ones have been produced by the formation of new separating lines of cement-substance. (See Fig. 204.)

Of particular interest is the condition of the hair-follicles and sweat-glands which are imbedded in the tumor. Many hair-follicles, still holding hairs, presented no material change; in others, the hair was wanting and the connective tissue of the follicle was transformed, in part at least, into the tissue of the tumor. The elements of the outer root-sheath were divided into

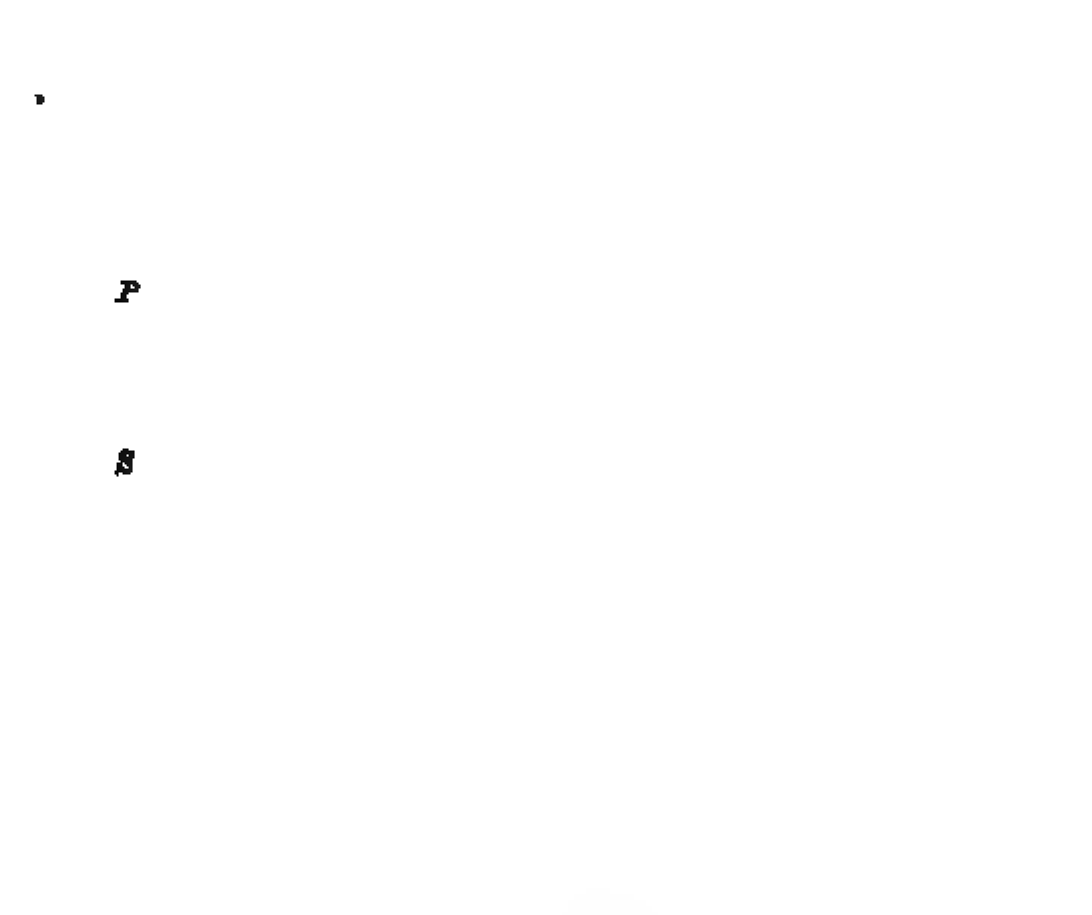


FIG. 205.—SURFACE OF A MYELOMA IN THE RIGHT GROIN OF AN ADULT.

M, partial wasting of cement-substance; *P*, thickened spokes (prickles); S^1, spindle-shaped plastids replacing the cement-substance; S^2, transition of the spindles into the frame of the myeloma tissue. Magnified 600 diameters.

glistening, brownish-yellow lumps, whose groupings indicated their origin from epithelia. All these bodies were interconnected by fine filaments. The ducts of the sweat-glands remained unaffected in most instances; but the glands presented a conglomeration of bright-yellowish bodies, which by their clustered arrangement indicated their origin from glandular epithelia. In many tubules seen in transverse sections the central caliber was absent, and in some places the bounding (structureless) layer of connective tissue was also gone, and the tissue of the tumor came in direct contact with the changed epithelia.

The skin covering the tumor (2) gave no evidence of ulceration, but was merely stretched, attenuated, and reddened. In vertical sections peculiar changes were noticed in the epidermal layer, which was reduced to a few layers of epithelia of the rete mucosum. Near the surface several epithelia were found coalesced, owing to the entire disappearance of the separating cement-substance. The "prickles" traversing the lines of cement-substance were well marked, even enlarged into oblong or square granules. In other places, instead of these granules, spindle-shaped or oblong bodies were seen, repre-

ES

L

S

FIG. 206.—GLOBO-MYELOMA, COMPOSED OF SMALL PLASTIDS. TRANSVERSE SECTION OF A SEMINIFEROUS TUBULE.

E, unchanged columnar epithelia; *ES*, commencing transformation of epithelia into myeloma elements; *S*, completed transformation of epithelia into myeloma elements; *L*, caliber of the seminiferous tubule. (For low amplification of the same tumor see Fig. 192.) Magnified 800 diameters.

senting what Biesiadecki termed "migrating cells." Careful observation, however, revealed that all of these bodies were connected with the neighboring epithelial elements by means of delicate filaments. Such formations were particularly numerous along the border separating the epithelia from the

myeloma-tissue, and many of the spindle-shaped bodies merged into the fibers separating the groups of myeloma elements. Here, therefore, a new formation had arisen mainly from the "prickles," while a direct transformation of epithelia into myeloma elements could not be demonstrated. (See Fig. 205.)

Transformation of epithelium into myeloma elements. The tumor of the testis (3) clearly exhibited the changes of the epithelia of the seminiferous tubules caused by the growth of the myeloma. Even low powers of the microscope demonstrated that the myeloma tissue had in numerous places pushed apart the seminiferous tubules, which in other places were entirely lost. In a number of specimens, not only the boundary layer of the tubules — toward the epididymis —was found to have disappeared, but the glandular epithelium itself presented, in part at least, features identical to those of the tumor. (See Fig. 193.) Higher amplifications explained satisfactorily this peculiar condition. The epithelium, in a transverse section of the tubule, appeared in part to be well preserved, while in another portion of the same tubule some of the epithelia exhibited coarse granules and solid lumps the size of nuclei. A striking feature was that in one epithelium an unchanged portion was found, and another portion was in the condition above described. Finally, there were portions in which the epithelium was replaced by myeloma tissue, in which its gradual stages could be traced. The increase of the living matter first gave rise to the formation of coarse granules and new nuclei; next, new boundary lines originated within the epithelia, dividing them into elements which bore no resemblance to the epithelia. Finally, the newly formed elements were partly infiltrated with basis-substance, the perinuclear form of which is characteristic of embryonal and lymph-tissue, as well as of certain so-called "small-cellular" varieties of myeloma. (See Fig. 206.)

The result of these changes is a real and complete transformation of the epithelia into myeloma tissue. Here and there I met in this tissue groups composed of 6-12 epithelia, which in all evidence were remnants of former glands or ducts, but not a glandular new formation. In all specimens of this tumor the spindle-shaped bodies which sprung from the cement-substance were in distinct connection with the reticulum of the myeloma tissue; and all formations of living matter (granules, nucleoli, nuclei, spindles, and trabeculæ) were interconnected by delicate filaments. Even in the perinuclear, mucoid basis-substance, in some places the bioplasson reticulum could be seen without the aid of re-agents.

In the case (5) I obtained a distinct view of the *changes of the liver-epithelia in growth of myeloma.* Low powers of the microscope proved that the newly formed myeloma nodules were separated from the surrounding liver-tissue by a tolerably thick capsule of connective tissue. Inside the capsule was a myeloma of alveolar structure; outside of it tracts of liver-epithelia were compressed, spindle-shaped, and running in a direction parallel to the surface of the capsule. In some places the boundary line between myeloma and liver-tissue was not sharply marked, but merely indicated by delicate bundles of connective tissue. Probably, these were the myeloma nodules of later periods. (See Fig. 207.) Here, in some places, the tracts of the liver-epithelia were well preserved, while in other parts the epithelium was broken up into globular or irregularly shaped bodies, which could only have originated from the living matter in the epithelium. These bodies presented all the stages of transformation into myeloma tissue; for, upon approaching the myeloma nodule, they were seen in groups, which, by virtue of their shape,

must be pronounced myelomatous alveolar formations, separated from each other by scanty connective tissue. Here, also, the endogenous production of living matter in liver-epithelia had led to the formation of myeloma tissue. The brownish color of the liver epithelium gradually faded into the grayish-yellow of the myeloma nodules. In like manner, the gradual transformation was indicated by the degree of carmine-staining, which had no effect upon unchanged liver epithelium, but became more intense with the deviation of the newly formed tissue from normal type of epithelium.

I can add that the myeloma of the submaxillary gland (4) presented, in some portions, analogous appearances. In this tumor, too, the transformation of the epithelium of the acini of the salivary gland could be traced, step by step.

My researches, in brief, gave the following results:

The myeloma growth, in its progress toward the epidermis, produces a change in the living portion of the epithelium similar to that which is observed in the superficial inflammatory processes of the skin. The cement-substance is dissolved; multinuclear bioplasson bodies arise, and in them new lines of division originate, producing indifferent elements, resembling those which spring from connective tissue. New elements are also produced by a new formation of living matter, both within the epithelia and in their cement-substance investment; in the latter situation, of course, from the filaments or "prickles" of living matter. Such a new formation

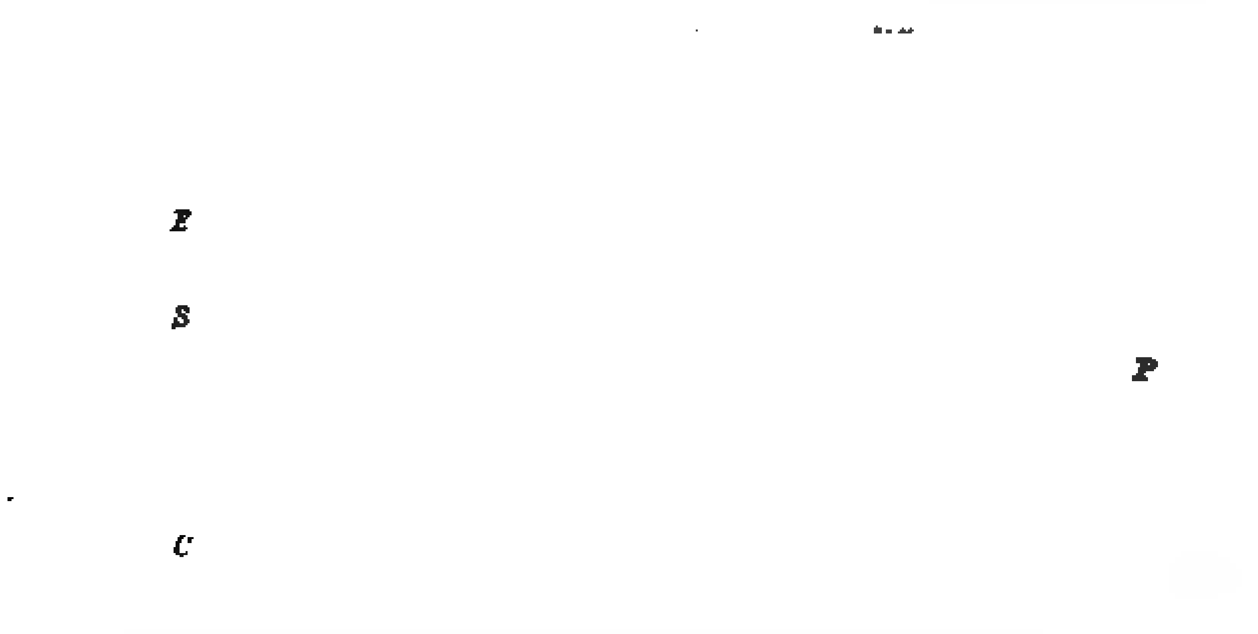


FIG. 207.—SECONDARY MYELOMA OF THE LIVER.

C, connective tissue which separates the myeloma nodule from the liver-tissue; *E*, little changed liver-epithelia within the myeloma nodule, *S*, new formation of myeloma elements from liver-epithelia; *P*, remnants of portal vessels. Magnified 600 diameters.

occurs in the epithelia of the external root-sheath and of the sweat-glands. The attenuation of the epidermis is evidently caused by a gradual transformation of the epithelia of the rete mucosum into myeloma tissue. In myelomata of glandular organs,—salivary glands, testes, liver,—the new formation of bioplasson starts in the epithelia with the appearance of new marks of division, and newly formed myeloma elements. The living matter of epithelium is directly converted into myeloma tissue, with a partial or complete destruction of the epithelia.

6. Lipoma. Fatty Tumor.

Lipoma is composed of fat-tissue, exhibiting a lobular structure and traversed by septa of connective tissue, which carries the blood-vessels. In the so-called *soft, fatty tumors* the connective tissue is scanty and the fat of a more oily nature, while in tumors termed *fibrous lipoma* (formerly called steatoma) the frame attains considerable development and the fat is more solid. The fat-globules resemble those of normal fat-tissue, and like these sometimes contain needle-shaped crystals of "margaric acid." (See Fig. 208.)

Lipoma appears as a tumor *sui generis* in the subcutaneous, submucous, and subserous tissues, rarely in glandular organs.

Fig. 208.—Lipoma, from the Shoulder of a Man.

V, capillary blood-vessel in the frame of connective tissue; *F*, fat-globules, pierced by vacuoles, the latter being caused by preservation in chromic acid. Magnified 400 diameters.

In the subcutaneous tissue it occurs usually on the posterior aspect of the body, and produces single globular, highly elastic tumors, the surface of which appears to be lobulated to the touch, and which, in different localities, have different degrees of consistency. The tumor is usually quite movable, and sometimes is very loosely attached to the body, pendent like a bag. The covering integument is either unchanged or it is thickened and pigmented, but may, as a rule, be raised in folds; it becomes

attached to the tumor only after injuries from without—f. i., friction of the clothing or long-continued pressure. Under these circumstances ulceration even may be produced, which is characterized by the offensive odor of discharge.

In the subcutaneous tissue both solitary and multiple fatty tumors occur; they may be circumscribed or diffused. Pedunculated and diffused fatty tumors are exceptional; the latter are of a softer consistency, and are attached to the skin by means of dense, fibrous connective tissue.

Lipoma is painful only when nerve branches are involved in the growth, and disturbance of functions is caused only by its size and weight. The growth is slow but almost indefinite, as there have been observed fatty tumors of twenty to thirty pounds. The larger the tumor the more marked is its lobular structure. Not infrequently calcareous deposition is found in the connective-tissue frame, and occasionally, though rarely, ossification.

Lipoma occurs combined with:

Hypertrophy of a finger, a toe, or the entire hand or foot;

Myxoma, fibroma, and myxo-fibroma, producing tumors of the skin, termed "nævus lipomatodes";

Cavernous angioma (Billroth), when especially the veins are ectatic in a high degree;

Myeloma, usually myxo-myeloma of the subcutaneous tissue.

Peculiar branching growths of serous membranes, especially of the knee-joint, which consist of delicate papillary vegetations of connective tissue, whose meshes contain fat-tissue, are considered as formations of lipoma (l. arborescens). Localized, diffuse new formation of fat occurs in the female breast, which, on one or on both sides, may reach an enormous size and weight.

7. Angioma. Vascular or Erectile Tumor.

The characteristic feature of angioma is an abundant supply of blood-vessels—arterial, venous, or capillary. This causes its erectility—*i. e.*, its swelling on a spontaneous engorgement of the vessels. Such tumors yield readily to pressure, but as soon as the pressure is removed they refill. In former times many of these tumors were termed "teleangiectasis," as they were thought to be due to a mere dilatation of the vessels; now we are ac-

quainted with the fact that the blood-vessels are really new formations. We can distinguish three varieties of angioma, according to the nature and distribution of the blood-vessels—simple, lobular, and cavernous angioma.

(a) Simple angioma is, to a great extent, composed of newly formed capillary blood-vessels, between which, in more or less uniform distribution, is a varying amount of fibrous or homogeneous connective tissue. The coat of the blood-vessels is composed of very large nucleated, sometimes stratified, endothelia; numerous tracts are solid, and composed entirely of endothelia (endothelioma). Both in the endothelia and the connective-tissue frame there are indications of a new formation of red blood-corpuscles, through the intermediate stage of hæmatoblasts. (See Fig. 209.)

FIG. 209.—SIMPLE ANGIOMA, FROM THE SKIN OF THE FOREHEAD OF A CHILD.

L, longitudinal section of a capillary; *S*, solid cord of endothelia, *F*, frame of a nearly homogeneous connective tissue. Magnified 600 diameters.

(b) Lobular angioma is composed of coils of large capillary blood-vessels, held together by delicate fibrous tissue, while between the coils this tissue is somewhat denser. The lobate structure is sometimes marked to the naked eye. In sections, the blood-vessels are cut in longitudinal, oblique, and transverse directions, and are found either empty or filled with blood. The capillaries are connected with large arteries or large veins, and the blood in the angioma may be clinically recognized as being of either venous or arterial character. (See Fig. 210.)

(c) Cavernous angioma is constructed on the plan of cavernous tissue—*i. e.*, composed of venous sinuses, which lie close to each other, separated only by walls of fibrous tissue, in which are capillary blood-vessels, and sometimes bundles of smooth muscle-fibers. The cavernous sinuses are filled with blood-corpuscles, and the blood has in its clinical aspect a venous

character—*i. e.*, is dark purple or bluish-red. The sinuses are lined with a delicate layer of endothelia. (See Fig. 211.)

Angioma is a common type of tumors, and in most instances is congenital. The simple and lobular angioma is located either in the tissue of the derma of the skin or in the subcutaneous tissue, and is in the latter situation abundantly supplied with fat-globules. These tumors may occupy large districts in the face (the so-called "fire-mole," nævus vasculosus), or they may appear in a number of smaller spots or elevations in different parts of the skin. They may either remain stationary or gradually increase in extent. Spontaneous cure is not an infrequent

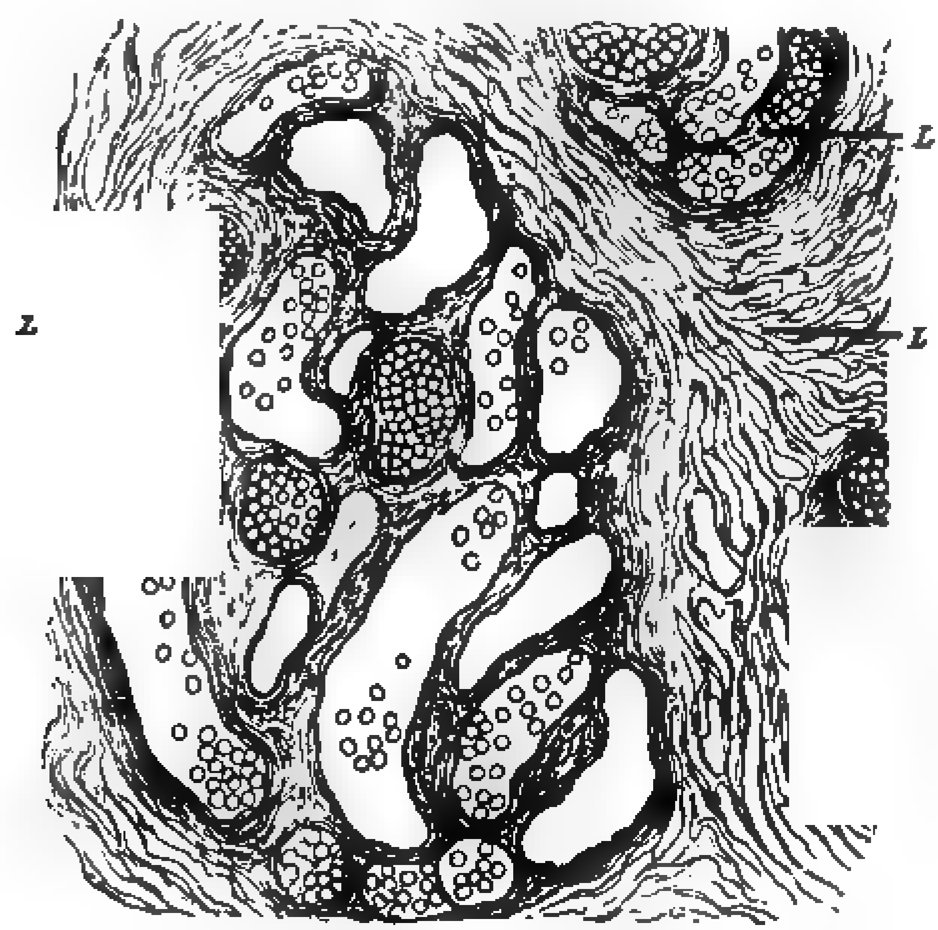


FIG. 210.—LOBULAR ANGIOMA, FROM THE ORBIT OF A CHILD.

LL, lobules composed of coils of large capillary blood-vessels, *I*, interstitial dense fibrous connective tissue. Magnified 350 diameters.

occurrence. The lobular angioma is, as a rule, more deeply situated than simple angioma; the tumor is to the naked eye marked by shallow, irregular nodulations of the surface. Upon invading the derma, the thinned skin covering it becomes immovable, and sometimes spontaneous ulceration takes place, though the hæmorrhage is rarely profuse. Cavernous angioma is somewhat rarer, and appears either as a sharply circum-

scribed, as if encysted, or as a diffuse tumor in the subcutaneous tissue, in muscles beneath the covering fasciæ, in the liver, the spleen, and the kidneys. It grows very slowly, and is often painful. The pain may be continuous or be due to pressure from without, and by rupture it may produce a dangerous hæmorrhage. Cavernous angioma reaches its highest development on the extremities, on single fingers, or as numerous scattered nodules, combined with considerable hyperplasia of the derma. Occasionally, though rarely, angioma involves mucous membranes. Several cases of angioma in the larynx have been reported. In rare cases, all the soft tissues of an extremity are transformed into the cavernous structure, with a gradual wasting

FIG. 211.—CAVERNOUS ANGIOMA, FROM THE BASIS OF A POLYPUS GROWN AT THE BORDER OF THE POSTERIOR NARES OF A CHILD.

T, trabeculæ of fibrous connective tissue, holding capillary blood-vessels; *E*, endothelial lining of the cavernous spaces; *B*, red blood-corpuscles. Magnified 700 diameters.

of the bone. Primary tumors of this kind, grown from the periosteum, and which gradually transform the bone into their own tissue, the so-called "pulsating bone-tumors," are rare. Angioma combines with myxoma, fibroma, lipoma, and adenoma.

Angioma may be composed of lymph-vessels, and is then termed *lymph-angioma*. There are two varieties: the *simple lymph-angioma*, composed of dense fibrous connective tissue, containing a

varying number of lymph-vessels (Hebra), and the *cavernous lymph-angioma*, composed of a large number of sinuous lymph-vessels and a comparatively scanty amount of connective tissue. Simple lymph-angioma is not of rare occurrence in the tissue of the skin, and usually appears in the form of numerous hard, compressible tumors the size of a lentil or of a hazel-nut. Cavernous lymph-angioma is rare, and, as a rule, deeply situated in the subcutaneous or subfacial tissue, producing sometimes very large tumors. Ulceration of these tumors occasionally takes place, with a continuous oozing of lymph. (See Fig. 212.) In *macro-*

FIG. 212.—CAVERNOUS LYMPH-ANGIOMA, FROM THE LATERAL REGION OF THE NECK OF AN ADULT.

C, frame of connective tissue, of a homogeneous, waxy appearance and a high refractive power; *F*, irregular reticulum of coagulated fibrine; *L*, lymph-corpuscle. Magnified 500 diameters.

glossa,—the congenital enlargement of the tongue, of mainly its anterior portions,—the mass consists of a fibrous connective tissue with numerous sinuous lymph-vessels, and is, therefore, cavernous lymph-angioma (Virchow). In some cases, cavernous blood-angioma was observed. No new formation of striped muscles was found in the tumor.

Attention has recently been drawn to tumors which, in addition to well-developed fibrous connective tissue, contain tracts or alveoli filled with finely granular polyhedral nucleated plastids, resembling the endothelia of blood-vessels. Tumors of this structure are termed *endothelioma*, and, as a matter of course, are of a benign character. I have seen such formations in a sebaceous adeno-fibroma of the scalp, in a lipo-fibroma of the skin of the face, and in a tumor of the choroid the size of a sugar-pea. Endothelia are in their structure identical with the medullary corpuscles, representing the stage of indifference from which connective tissue and its derivations arise. In the first instance, the endothelial tracts were like blood-vessels, but without perforation; such tracts were also observed in the angioma of the skin of the forehead of a child, illustrated in Fig. 209. In the second case, fat-globules were found in the midst of the endothelia, and the conception was admissible that fat originated from the endothelia, there representing an intermediate stage. In the third case, alveoli were present, closely resembling cancer nests. The differential diagnosis in such a case rests upon the regular arrangement of the alveoli; the lobular structure of the tumor; the fully developed fibrous connective-tissue frame, which is of a nearly uniform width and scantily supplied with blood-vessels; the fine granulation of the plastids and their pale, finely granular nuclei. In such cases a positive differentiation between endothelioma and epithelioma (cancer) seems difficult, if not impossible; though the clinical course of the benign endothelioma is altogether different from cancer.

8. Myoma. Muscle Tumor.

Tumors composed exclusively of striated muscles do not occur; striped muscle-fibers are constituents of tumors, appearing occasionally in the testis and the ovary, which also contain remnants of other tissues, such as cartilage, bone, teeth, and hairs. These are the so-called "dermoid cysts"—teratoid and combination tumors. On the contrary, tumors composed of smooth muscle-fibers are of frequent occurrence, always combined, however, with fibrous connective tissue, constituting, therefore, myo-fibroma or fibro-myoma. The organ which is the most frequent site of tumors of this sort is the uterus, in middle and advanced age, especially in the colored races.

Myo-fibroma of the uterus appears either beneath the mucous layer, in the middle of the wall, or at the periphery of the uterus (submucous, intraparietal, and subserous myo-fibroma), and in almost every instance more or less smooth muscle-fibers are found mixed with the connective tissue. The latter tissue carries the blood-vessels, which vary greatly in amount and sometimes are so abundant as to justify a diagnosis of *angio-myoma*. Fibrous tumors of the ovaries which I have examined exhibited the same features. A subserous myo-fibroma of the uterus, under the microscope, gave the appearances illustrated in Fig. 213.

The bundles of smooth muscles are either scattered irregularly throughout the tumor, always interlacing in different directions, as shown by sections, or there is a lobular structure when nodules containing many smooth muscles, but little connective tissue, are separated from each other by comparatively broad layers of fibrous connective tissue. In bundles of smooth muscle-fibers, cut longitudinally, the muscle nature of the fibers is often unrecognizable, as they blend with those of connective tissue, while in transverse sections of the bundles all doubts of the

FIG. 213.—MYO-FIBROMA OF THE UTERUS.

L, bundles of smooth muscle-fibers cut longitudinally; *F*, bundles of smooth muscle-fibers cut transversely; *A*, artery with a very broad muscle-coat; *V*, vein. Magnified 200 diameters.

muscle nature of the fibers are removed, owing to the presence of abundant bioplasson and rod-like nuclei within the spindles, separated from one another by a delicate fibrous perimysium. One of the most striking features, in some cases, is the heavy muscle-coat surrounding the arteries. (See Fig. 214.)

Myo-fibroma of the uterus is prone to fatty and calcareous degeneration; the former invades both the plastids of the connective tissue and the muscles, the latter only the connective-tissue frame. Moreover, there are cases on record where an original myo-fibroma has changed into a malignant myeloma, or even into cancer.

Myoma is a tumor of rare occurrence in the skin (growing in the neighborhood of the nipple and in the scrotum), somewhat less rare in the wall of the œsophagus, the stomach, the intes-

F

FIG. 214.—MYO-FIBROMA OF THE UTERUS.

L, longitudinal bundles of smooth muscle-fibers, not distinguishable from fibrous connective tissue; *F*, bundles of smooth muscle-fibers, cut transversely; *A*, artery with a heavy muscle-coat. Magnified 500 diameters.

tines, in the wall of the urinary bladder, and in the prostate (in the latter, hyperplastic myoma—Virchow).

9. NEUROMA. NERVE TUMOR.

The term "neuroma" can be properly applied only to tumors which consist entirely, or at least partially, of newly formed medullated or non-medullated nerve-fibers; but it is doubtful

whether such formations ever occur. Tumors containing nerves have been observed most frequently on the spinal nerves, less frequently on the sympathetic, and least frequently on the cerebral nerves. No positive proof has been given, however, that the great quantities of nerves in these tumors are really newly formed. If the internal perineurium—of course connective tissue only—be augmented, the innumerable nerve-fibers are pushed apart and may make the impression of constituting a true neuroma. Günsburg, Wedl, and others have demonstrated that, in the nodular nerve-growths developed after the amputation of a limb, large numbers of the bundles of nerve-fibers, both of the medullated and non-medullated varieties, were newly formed. There are recorded cases in which one nerve produced a number of tumors, which gave the formation a rosary-like appearance; in other cases, on a number of nerves in different localities, tumors were found, and it is asserted that in such nodules newly formed nerves were present in a large number (myelinic neuroma of Virchow). Some congenital tumors in the sacral region have been found to contain a large number of medullated nerves. Virchow observed teratoid tumors, composed of nerve-tissue, resembling the gray substance of the brain.

Of still more doubtful occurrence are the tumors composed of non-medullated nerve-fibers,—the amyelinic neuroma of Virchow,—who describes a case of recurrent ulcerative, and consequently malignant, neuroma ("neuromatous diathesis"). Even with our modern methods of investigation a positive proof of the presence of non-medullated nerve-fibers is not easily obtained, and many authors have doubted the existence of true amyelinic neuromata.

Most of the nerve tumors have proved to consist, in addition to a varying number of nerve-fibers, of the myxomatous and fibrous varieties of connective tissue. Instead of using the term "spurious neuroma," we shall designate such tumors as myxoma or fibroma growing from a nerve, or if the tumor contains a large number of nerve-fibers, we may term it neuro-myxoma, or neurofibroma. Most of the so-called "painful tubercles" of the skin also belong to this class. (See Fig. 215.)

Sometimes myeloma develops on or in a nerve, and, in accordance with our terminology, such a tumor would be called neuro-myeloma. The nerve-fibers, however, in the advancing growth of the tumor are soon destroyed and transformed into myeloma tissue.

The most important clinical sign of neuroma is its painfulness, which bears no relation to its size. Small tumors the size of a lentil are sometimes extremely painful, while large ones, the size of a man's fist, cause little or no pain. This difference in the amount of pain depends, doubtless, upon the fact that the nerve-fibers in some tumors are quickly destroyed or transformed into the tissue of the tumor.

10. Papilloma. Warty Tumor.

Warty tumors are combinations of connective and epithelial tissue; the former produces the finger-like, papillary elevations, the latter furnishes the outer investment. The connective tissue

Fig. 215.—Neuro-fibroma of the Skin above the Patella of a Woman.

N, remnants of medullated nerve-fibers, with fluted outlines; *M*, myeline drops, separated from one another; *V*, capillary blood-vessel. Magnified 600 diameters.

is in its structure either fibrous or myxomatous, or a combination of both, and, as a rule, supplied with numerous blood-vessels, some of which are very large. Sometimes papillomatous growths exhibit the structure of myeloma, either from the beginning or after, by repeated trials of extirpation, considerable irritation has

been set up. Under these circumstances, an originally benign papilloma may pass into a myeloma, or a secondary change into cancer may take place, both rendering the tumor malignant. According to the nature of the connective tissue and the amount of covering epithelium, we distinguish a horny and a myxomatous papilloma as primary tumors.

(a) Horny papilloma is composed of highly vascularized fibrous connective tissue, producing branched, finger-like prolongations, and is covered by a stratified epithelial layer, usually of considerable breadth. The deepest layers of the epithelia contain a varying amount of pigment. (See Fig. 216.)

FIG. 216.—PAPILLOMA OF THE LARYNX.

E, heavy epithelial cover; *P*, papillary prolongations of connective tissue; *V*, wide blood-vessels. Magnified 50 diameters.

Warty tumors are of frequent occurrence on the skin, particularly of the fingers, and are often caused by a continued local irritation of the part. They usually appear at the time of puberty, and disappear spontaneously. They attain the largest size in the region of the genitals, and are called in this situation warty condylomata, their growth being always due to the local irritation produced by the blennorrhoic secretion. They have nothing in common with syphilis. Warty tumors are also of frequent occurrence in the mucous membranes, especially of the

larynx. The *horns* and *claws* of the skin of the face and the scalp of elderly persons are papillomatous tumors with very long and thin papillæ. Warty tumors are known to be difficult to cure, and with advancing age sometimes to change into cancer.

(b) Myxomatous papilloma occurs rarely on the skin, but more frequently on mucous membranes. Such tumors consist of a soft myxomatous connective tissue, always rich in blood-vessels, and covered either with a comparatively thin layer of stratified epithelia, or with a single layer of columnar epithelium. (See Fig. 217.)

P^3

P^4

P^5

FIG. 217.—PAPILLOMA OF THE MUCOSA OF THE UTERUS.

P^3, papilla covered by a single layer of columnar epithelia; P^4, epithelial layer in top-view, P^5, papilla deprived of its epithelial cover. Magnified 600 diameters.

To this class belong the papillomatous tumors, so-called "carunculæ," of the female urethra, which are often extremely painful and cause serious hæmorrhages. They appear as dendritical, scarlet, sessile vegetations, usually at the external orifice of the urethra. They occur, but are rare, in the mucosa of the uterus and of the bladder. Lücke first drew attention to the fact that the formerly so-called "papillary cancer" of the bladder is originally a benign papilloma, which in a secondary change may take on the charac-

ter of myeloma or cancer. This fact was recently corroborated by the accurate investigations of A. W. Stein. Papilloma of the uterus may cast off portions of its substance with the menstrual discharges. This occurred in the case of the woman who passed the shreds illustrated in Fig. 217. Shreds of tissue may also be passed with the urine, if papilloma of the bladder be present. Papillary tumors combined with adenoma sometimes appear in other mucous membranes, and they are always more difficult to eradicate and more prone to change into a malignant type than simple myxo-adenoma.

Microscopical Study of Papilloma of the Larynx.

By Louis Elsberg, M. D., New-York.*

All other laryngeal tumors together occur less frequently than papillomata. Of three hundred and ten cases of intralaryngeal morbid growths that have come under my observation, I believe one hundred and sixty-three to have been papillomatous, although the diagnosis, many times, was made clinically only—*i. e.*, without microscopical examination.

The tumor, the size of a coffee-bean, which is the subject of my study, was removed by evulsion from the anterior portion of the vocal band of a woman thirty-six years old. In sections examined with low powers of the microscope a central mass of connective tissue is seen, abundantly provided with large blood-vessels, mainly veins and capillaries, some choked with blood. Tapering prolongations extend from this mass outward toward the periphery of the tumor and the papillæ, and terminate in a large number of minute, finger-like ramifications. The central mass, with its prolongations, is invested with a thick stratified epithelium, the lowest portion of which—*i. e.*, the one nearest the connective tissue—is a row of columnar epithelia, the main mass cuboidal, and the peripheral portion flattened epithelia. The latter exhibit in some places irregular erosions, which produce a rather jagged outline. Corresponding to the papillæ, the epithelial layers form rounded protrusions, the valleys between the papillæ representing the main mass of epithelial structure.

Higher powers of the microscope (500–600 diameters) show the fibrous connective tissue in the central portion of the tumor to be made up of interwoven, longitudinal, and transverse delicate bundles of fibers, the relatively thinner bundles being nearer the periphery. Most of the papillæ contain predominantly the variety of connective tissue called myxomatous. Within the connective-tissue bundles are seen numerous plastids, either single or in chains, either roundish or oblong and fusiform, which are the so-called connective-tissue corpuscles. In the myxomatous portion the fibers are more delicate than in the fibrous, and are in many instances arranged in the shape of a delicate net-work, at the nodes of which small, oblong nuclei are met with, while the meshes contain either a finely granular basis-substance or globular plastids of varying size. The blood-vessels, which, as before mentioned, are very numerous and very large, wind their way between the bundles, and some of them

* Abstract from the author's essay, "Archives of Laryngology," vol. i., 1880.

have a very narrow but distinct muscular coat. The endothelial coat of the capillaries is well developed; at some places the endothelia are clustered together, with marks of division within the cluster, pointing to a proliferation of the endothelial wall. Most of the capillaries are surrounded by a somewhat denser fibrous connective tissue, even in the myxomatous portion of the tumor. This layer of fibrous tissue constitutes an adventitia of the capillary blood-vessels more distinct than is ordinarily met with in normal tissues.

The boundary-line between connective tissue and epithelium at many places in the various specimens is sharply defined by a narrow zone of dense fibers, identical with what has been termed the basement membrane; at other places, on the contrary, such a bounding zone is absent, and there is a gradual transition of connective tissue into epithelium. In the latter cases the epithelial bodies send offshoots into the reticular portion of the myxomatous tissue, and it is impossible to tell where one terminates and the other begins. Where a bounding layer of connective tissue exists, the columnar epithelia are well defined; where such a zone is absent they are ill defined, several rows being sometimes piled up, each epithelium of a more or less fusiform shape and very narrow. Surrounding each individual epithelial body, whether spindle-shaped or well defined, and separating each from all the others, there are very narrow light rims, pierced by extremely delicate threads. The main mass of epithelium consists of cuboidal elements, which are polyhedral and separated from each other by a light rim,—the so-called cement-substance,—traversed by a large number of delicate threads or "thorns." Whenever the razor has reached the surface of a cuboidal element in front section, the epithelium looks as if studded with short hairs or thorns. The cuboidal epithelia nearest the outer limit exhibit the cement-substance and the thorns less markedly, and in the layer of flattened epithelium at the periphery, cement-substance and thorns are scarcely recognizable.

Most of the cuboidal epithelia hold in their interior a nucleus, the aspect of which is, however, various. Not infrequently an epithelium has two nuclei, of which one is finely, the other coarsely, granular, or both may be coarsely granular, differing from each other only in size and in the number of granules they contain. Occasionally a nucleus constitutes an almost homogeneous shining mass; and, again, a mass split up into two or three relatively large lumps or clusters of granules. Around compact nuclei a broad light rim is sometimes visible, evidently a vacuole—*i. e.*, a closed space filled with a liquid. Large vacuoles in the centers of some epithelia are seen perfectly empty, presumably because the nucleus that was in them has fallen out, or been dragged out by the razor.

Instead of the so-called thorns seen in cement-substance, frequently slender spindles are wedged in between two epithelia of a higher refracting power than the latter. Or a shining spindle-shaped corpuscle lies close against one wall of an epithelial body, while the cement-substance at the opposite side of the spindle is slightly distended, and pierced by thorns running at right angles to the spindle. In other instances, the thorns between two epithelial walls seem to have run together into an almost square or oblong homogeneous shining rod; the cement-substance, more or less broadened, surrounding the rod on one or both sides and being pierced with other slender thorns. Again, compact club-like or pear-shaped shining bodies, or a number of granules in clusters of either a pear- or spindle-shape, are seen in the considerably distended cement-substance between two epithelia. These masses sometimes

reach, and sometimes surpass, in size that of large epithelial nuclei. Lastly, pale or coarsely granular bodies are seen wedged in between two or three neighboring epithelia, smaller in size than the latter, some being devoid of, and some possessing, oblong nuclei. These various formations in the cement-substance are found in large numbers in the vicinity of the papillæ. They occur in the cement-substance of columnar as well as in that of cuboidal epithelia. Very near the periphery of the tumor they are scanty, but absolutely absent in the outermost layer of flat epithelium only.

With the highest powers of the microscope (1200 diameters) the fibrous portion of the connective tissue is seen to be composed of extremely delicate spindles, which are separated from each other by very narrow light rims, analogous to those which we are accustomed to see in epithelial formations. By closely watching these light rims we certainly detect in them slender threads, analogous to the thorns long known to exist in the cement-substance of epithelium. The spindles themselves, representing what we call basis-substance of connective tissue, are by no means homogeneous. In the thinnest layers of the bundles in the central portion of the tumor they exhibit a delicate but distinct net-work, the threads of which are grayish, the carmine coloring being confined to the meshes. Interspersed between the spindles is seen a large number of multi-caudate corpuscles of reticular structure, the peripheral sprouts of which tend toward the spindles and inosculate with the net-work of the basis-substance.

The peripheral portion of the connective tissue is, as has already been stated, of a prevailing myxomatous structure. Here the spindles constituting the basis-substance, instead of being packed together to form bundles, are associated in the shape of a coarse reticulum, holding numerous small corpuscles, mainly at the points of intersection; but the larger meshes encircled by the spindles also contain a number of similar corpuscles or else a light, so-called myxomatous, basis-substance. High powers of the microscope reveal a delicate net-work structure in the inside fields of the myxomatous basis-substance, as well as in the encircling spindles, and this net-work is in uninterrupted connection with the corpuscles at the junction of the spindles and those contained in some of the meshes.

The most peripheral portion of the connective tissue is in connection with the epithelium. Where a sharp line of demarcation exists, the highest powers of the microscope reveal a single layer of connective-tissue spindles, serving as a basis for the epithelia to rest on. This terminal stratum is in close connection with the subjacent reticulum of myxomatous tissue and with the capillary blood-vessels nearest the periphery. The blood-vessels not infrequently approach the stratum so near that only a very narrow light rim is left between their wall and the epithelium, and this rim is invariably traversed by delicate grayish filaments. On the opposite side the stratum is in close contact with the peripheral threads of the net-work of fully developed columnar epithelia. In the case of not fully developed epithelial elements, as intimate a connection is established by shining homogeneous spindle-shaped prolongations, which go from the terminal stratum into the epithelial layer as either an irregular reticulum or rows of filaments, arranged in a more or less regularly vertical direction around a reticulated corpuscle, containing in its interior one or more small, reticulated bodies of the aspect of nuclei. Thus, such a reticulated corpuscle —*i. e.*, a not yet fully developed epithelium—is inclosed in the spindle in a similar manner to that in which the cement-sub-

stance surrounds fully developed epithelia. The difference is that the spindles are homogeneous and shining, of the same refracting power as the granules and threads of living matter, while the cement-substance is a pale layer without any refracting power. Evidently, the spindles are compact masses of living matter from which future epithelia arise, while the cement-substance proper is a lifeless, horny material, containing only very little living matter in the shape of the minute thorns that traverse it.

Where there is no sharp demarcation between connective tissue and epithelium, even the highest powers of the microscope fail to demonstrate where one terminates and the other begins. Only the presence of capillary blood-

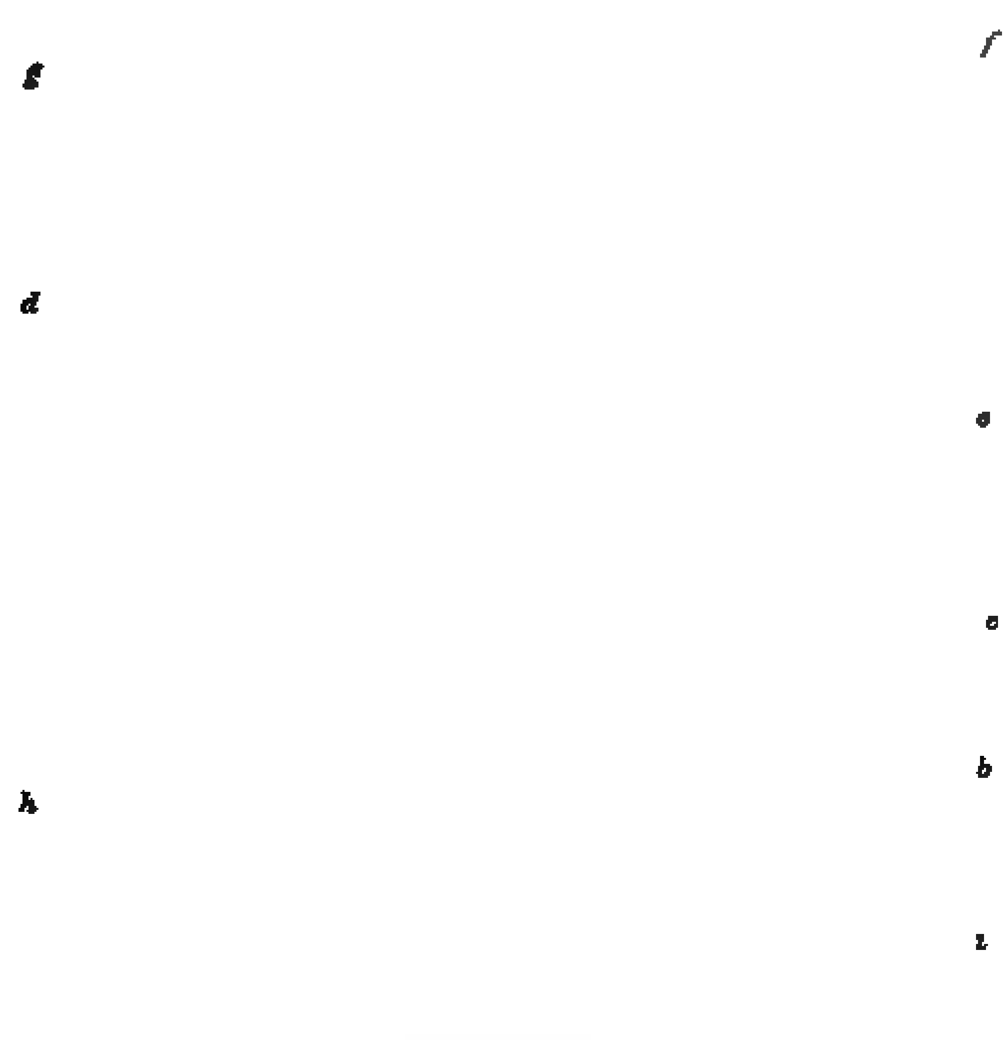


FIG. 218.—PAPILLA, WITH SURROUNDING EPITHELIUM. OBLIQUE SECTION.

a, bundle of fibrous connective tissue, *b*, plastid between the spindles, *c*, myxomatous connective tissue; *d*, capillary blood-vessel cut across; *e*, layer of connective tissue at the base of the epithelia; *f*, spindle-shaped prolongations of the layer *e*, insinuated between the epithelia, *g*, columnar epithelium; *h*, medullary tissue, transition of connective tissue into epithelium. Magnified 1200 diameters.

vessels furnishes some guidance for the determination of what is connective tissue. (See Fig. 218.)

In the lower strata of epithelia we most frequently meet with the appearances in the cement-substance already described. The high power

reveals in the cement-substance masses of living matter which tend unquestionably toward the formation of new epithelial bodies. The initial stage of such formation is a growth and confluence of the thorns into rods or spindle-shaped masses, which remain in connection with the neighboring epithelia by means of delicate threads. Such a change in the bulk of the living matter is possible only after the liquefaction of the horny cement-substance. An increase in the bulk of the thorns is invariably accompanied with a widening of the space occupied by the cement-substance. Of course, the larger the formations of living matter between the epithelia become, the larger must become the space in which they are located; and this enlargement often leads to the production of bay-like excavations along the walls of contiguous epithelia. Such excavations sometimes hold irregular clusters of bodies, which in their optical behavior are identical with the nuclei of epithelia generally. The preliminary stage in the development of a new epithelial body is completed by the appearance of a coarsely granular plastid, between the old finely granular epithelia and the appearance of lines of new cement-substance around the newly formed body. Changes similar to those that go on in the cement-substance also occur in the interior of the nuclei. Nuclei of a dumb-bell shape, or two nuclei within one epithelial body, have long been known as common features in epithelia. They certainly seem to point to a multiplication of nuclei, but I am unable to say whether they have anything to do with new formation of epithelia or not. (See Fig. 219.)

As an *addendum* I may state that I have found, in microscopical sections made from a papilloma of the penis, a so-called venereal wart, the same characteristic features that I have described as belonging to papilloma of the larynx.

A. Biesiadecki was the first to draw attention to the presence of shining, spindle-shaped bodies within the cement-substance of inflamed (eczematous) skin, in which an active new growth of epithelia takes place; but he claimed that these spindle-shaped bodies came from the connective tissue. The most recent writer, E. Klein, holds a similar opinion, for he describes and figures in his "Atlas of Histology," in the cement-substance of epithelium from the tail of a tadpole, what he calls "branched cells" of connective tissue, which "are seen to extend with their processes amongst the epithelial cells." My observed series disproves, of course, any such opinion.

What I have proved in regard to the new formation of epithelia is that: (1) *Epithelium multiplies from medullary elements not distinguishable from those that form connective tissue at the boundary between these two tissues;* (2) *epithelium multiplies from the new growth of medullary elements which originate in the living matter — the so-called thorns — within the cement-substance.*

11. Adenoma. Glandular Tumor.

Adenoma is composed of a myxomatous or fibrous connective tissue, containing newly formed glands of either the acinous or tubular varieties. Blood-vessels are found only in the connective-tissue portions. The most characteristic feature of the glands is the central caliber, which is invariably found in both the acinous

and tubular formations. Acinous glands, as a rule, are lined by cuboidal or short columnar epithelia, which are often stratified; while tubular glands are lined by columnar epithelia, which are sometimes ciliated. The regularity in the arrangement of the epithelia, their fine and uniform granulation, and the comparatively fine granulations of the nuclei, are, in many instances at least, distinguishing points for the diagnosis of an adenoma under the microscope.

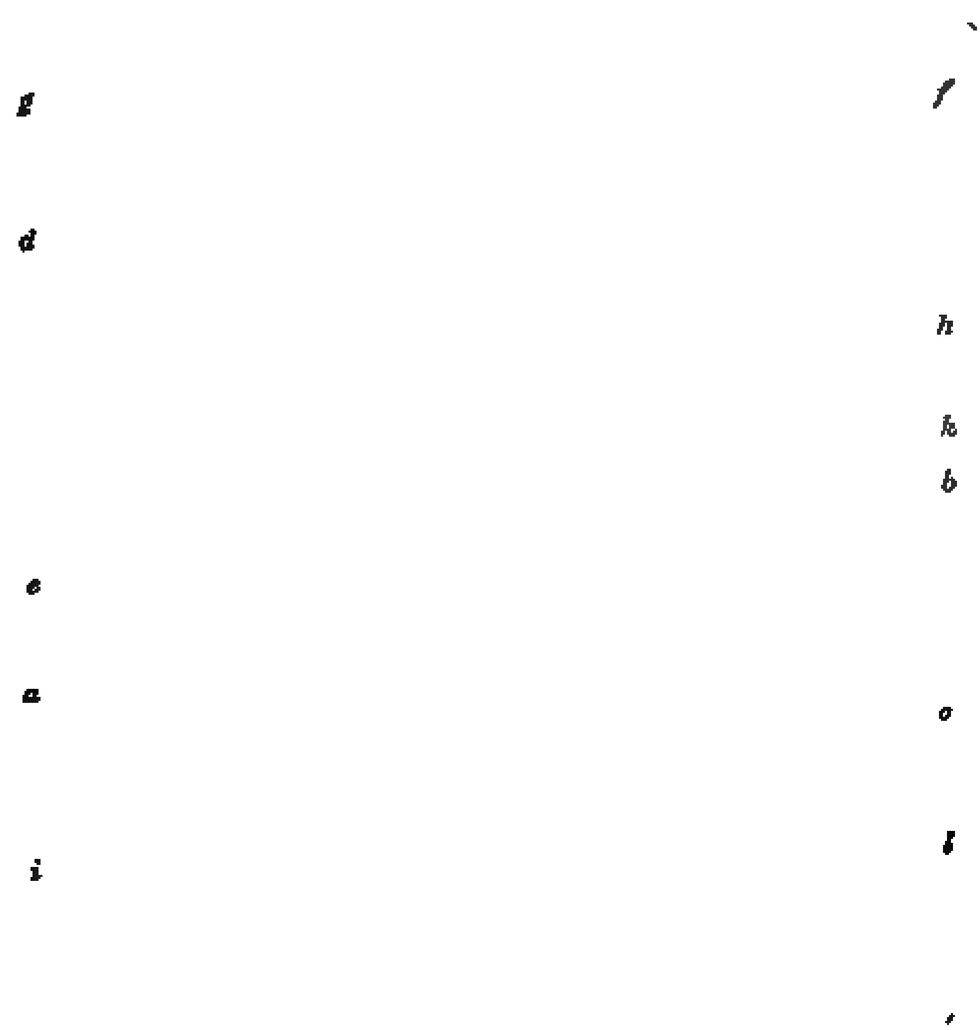


FIG. 219.—CUBOIDAL EPITHELIA, FROM THE NEIGHBORHOOD OF THE COLUMNAR EPITHELIA.

a, nucleus surrounded by a light space, a so-called vacuole; *b*, empty vacuole, nucleus dropped out; *c*, epithelium with two nuclei; *d*, epithelium with a bright, homogeneous nucleus; *e*, "thorns," or filaments of living matter in the cement substance; *f*, thorns increased in size; *g*, enlarged thorns, united into a shining, spindle-shaped body; *h*, pear-shaped body between epithelia; *i*, rows of lumps and rods; *k*, medullary elements; *l*, newly formed epithelium wedged in between the old. Magnified 1200 diameters.

Adenoma is a common tumor, and occurs most frequently in the following localities:

In the skin glandular new formations are observed, starting from the sebaceous glands as sebaceous cysts, as molluscum seba-

ceum, and as milium. In some instances the epithelia are transformed into large, shining, sometimes stratified, colloid corpuscles, which were erroneously thought to be the infectious material of the so-called *molluscum contagiosum*, when a number of smaller tumors form around a large adenoma. In milium the sebaceous mass is inspissated, and by deposition of lime-salts is transformed into cretaceous material. Tumors of this kind are often inclosed by a thick fibrous connective-tissue capsule; they are liable to become inflamed and ulcerated or to enter the cystic degeneration.

In *mucous membranes*, most of the myxomatous sessile or pedunculated so-called polypous tumors are adenomatous (Billroth), and deserve the name *myxo-adenoma*. They occur in the mucosa of the nasal cavities, the throat, the larynx, the tympanum, the rectum, and the uterus. In children, polypi occur most frequently in the rectum, while in middle-aged persons they are more commonly found in other localities. Their size varies greatly. Those of the rectum sometimes grow to be as large as a chicken's egg; those of the uterus reach a still larger size. Exceptionally a marked papillary character is observed on the surface. Rectal polypi show a distinct tubular structure in the newly formed glands. Ciliated epithelia occur both on the surface of the tumor and in the ducts of the glands, especially in polypi of the nasal, laryngeal, and aural regions. Those of the uterus also exhibit ciliated columnar epithelium, and are found both in the mucosa of the cervical canal and in that of the uterine cavity proper. In the latter situation they are often combined with the lymphoid variety of myxomatous connective tissue, representing a benign type of tumors, though sometimes occupying quite extensive tracts of the mucosa.

A larger number of medullary elements in the myxomatous connective tissue indicates a more rapid growth and greater proneness to recurrence after extirpation. Exceptionally a transformation into myeloma and cancer takes place, particularly after repeated attempts at eradication.

In the *female breast*, adenoma of the acinous variety is also of common occurrence, combined with myxoma or fibroma. Sometimes the tumor is circumscribed and sharply defined from the surrounding tissue; at other times the growth invades one or both mammary glands almost uniformly, which results in the formation of very bulky tumors. If the connective tissue is profusely provided with medullary elements, the growth becomes

an *adeno-myeloma*, which is often combined with cystic formations, and this condition was called *cysto-sarcoma mammæ.* In such tumors, well-marked cauliflower-like vegetations protrude into the calibers of the newly formed dilated and folded glandular spaces. These vegetations were erroneously supposed to be intraglandular; but they are obviously produced by an outgrowth of the connective tissue lying behind the glandular wall, which is usually extremely vascular, and pushes and folds the wall into peculiarly complicated prolongations. Adeno-myeloma of the breast sometimes breaks open and ulcerates, and the vascularized vegetations may bulge out from the ulcer, with a simultaneous rapid growth of the tumor. Nevertheless, this variety of tumor is known to be comparatively benign, and to admit of a permanent cure by extirpation.

In the *thyroid body* adenoma often occurs, producing the disease termed goitre. Either the alveoli, containing lymph-corpuscles and colloid material, are uniformly dilated—the so-called parenchymatous goitre—or some of the alveoli, still lined by the original embryonal epithelia, may become cystic and, in addition, be provided with numerous vascularized vegetations on the inner surface of the cyst—cystic goitre. From the alveoli cancer may also develop as a primary or secondary tumor.

The majority of cysts are secondary formations of adenoma. We sometimes observe cystic spaces in polypoid tumors, and can trace the gradual transformation of the glandular epithelia into a mucous, colloid, or serous mass. As an intervening stage, a sort of myxomatous tissue is observed arising from medullary corpuscles, into which the epithelia change before their liquefaction. The closed cavity of the original alveolus is gradually distended and becomes a cyst, the inside wall of which is lined by flat epithelia. (See Fig. 220.)

The *sebaceous cysts* and *milium* in the skin are invariably preceded by a stage of adenoma. In the subcutaneous tissue other cysts may arise independently of epithelial growth—f. i., the *meliceris*, a cyst with honey-like contents; the *hygromata*, cysts of the *bursæ mucosæ;* and the so-called *ganglia*, cysts of the sheaths of tendons. The cause of the appearance of cysts in such cases as these is not known. Obviously, the cystic formations which spring from an accumulation of blood, due to an extravasation, cannot be considered as tumors in the strictest sense of the word.

Unquestionably, epithelial growth produces the so-called *dermoid cysts*, which are very probably caused by anomalous forma-

tions in embryonal development — the formation of an imperfect fœtus in one perfectly developed, or intrauterine isolation by constriction of parts of the embryonal body. These cysts contain, besides epidermal tissue, hair-pouches, hairs, and also sebaceous and sudoriparous glands, cartilage, bone, and teeth. Such tumors were observed in the subcutaneous tissue, concreted with the periosteum, in the orbit and its vicinity, in the testes and the ovaries, rarely in other organs. Dermoid cysts have also been observed in the lateral regions of the neck, and, as has been

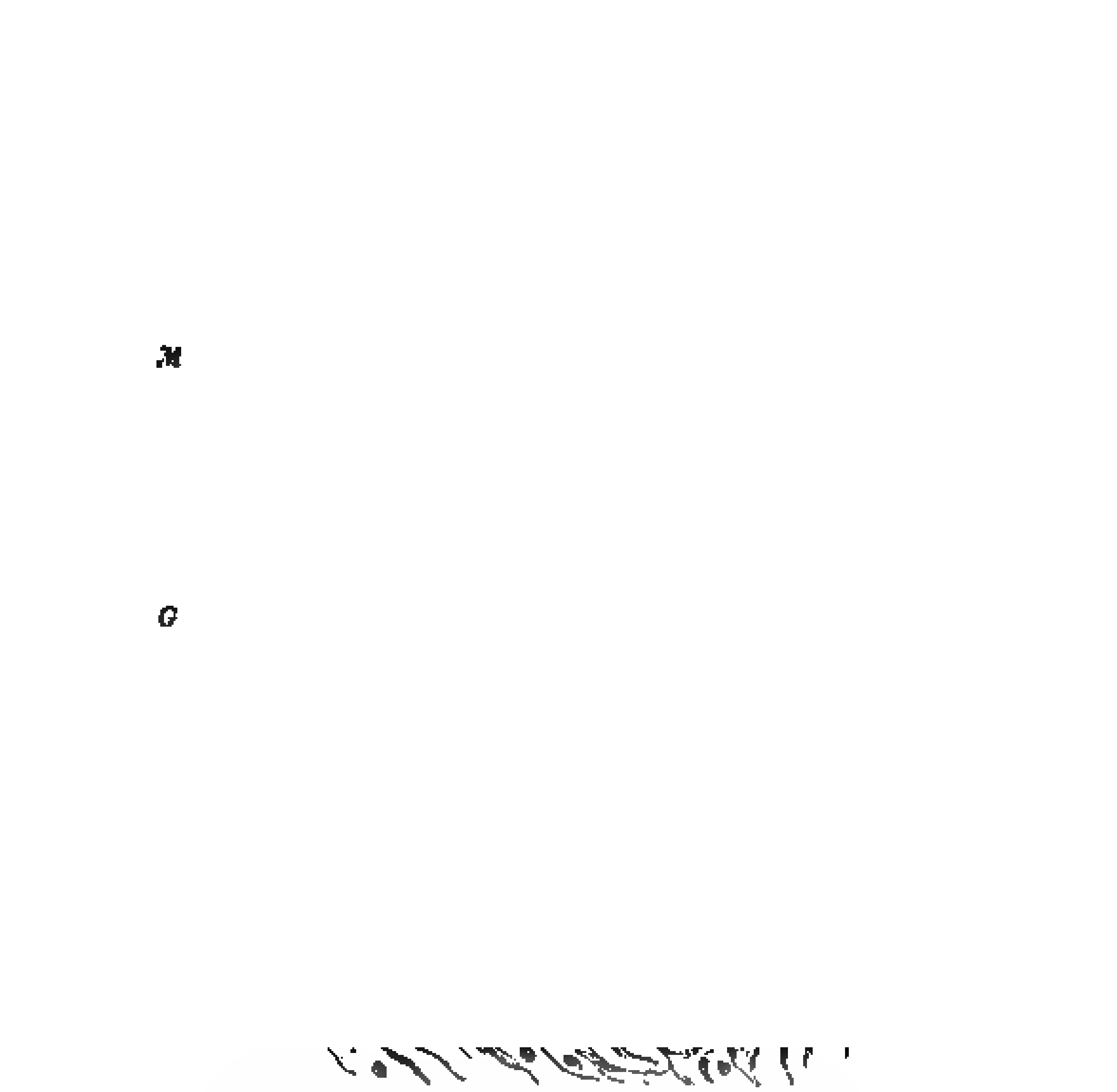


FIG. 220.—FORMATION OF CYSTS IN MYXO-ADENOMA. NASAL POLYPUS.

M, myxomatous connective tissue; *G*, mucoid degeneration of the epithelia of an acinous gland — a future cyst. Magnified 400 diameters.

suggested by Roser, are due probably to an imperfect retrogression of the gill canals of the embryo. Some of the cysts, occurring at the base of the oral cavity beneath the tongue, and termed *ranulæ*, are considered dermoid cysts, especially

when their contents are dry epidermal or fatty, sebaceous masses.

Cysts of the internal female genital organs are of frequent occurrence, usually found in the ovaries, and presenting either simple cysts inclosed by a comparatively thick capsule, or the so-called parenchymatous cysts, which are combined with adenoma or cancer (cysto-adenoma, cysto-carcinoma). The latter varieties are rare in comparison with simple cysts. They are composed of one sac only, or of a number of partly closed, partly confluent, cavities — the so-called multilocular cysts. Their contents are either a serous or a viscid colloid liquid, with a varying amount of blood. By a gradual change in the coloring matter of the blood the contents show varying shades of brown. An admixture of pus renders the liquid cloudy, and by decomposition it becomes offensive and ichorous. Whenever pus-corpuscles are present, as a general thing, we find large, coarsely granular bodies,— the so-called gorged corpuscles,— which, perhaps, are epithelia in fatty degeneration; while red blood-corpuscles, swelled, and robbed of their coloring matter, appear as pale bodies, containing only few granules; these are the so-called Drysdale's corpuscles, which are not characteristic, by any means, of the contents of an ovarian cyst. Cysts of the broad ligament also can be traced back to their epithelial origin from the parovaries; these single cysts almost always have very thin walls and serous contents, without any combination with solid tumors.

In ovarian cysts the origin of the closed sacs from previous glandular formations, in most instances, can be easily traced. Usually, cysts originate in organs containing epithelia,— f. i., the liver, the kidneys,— though here the cysts are, in the majority of the cases, produced by an inflammatory process. The medullary corpuscles springing from the former epithelia are specially endowed with the capacity of mucoid or colloid degeneration and the formation of secondary cysts.

12. Carcinoma. Cancer.

Carcinoma is composed of connective tissue and epithelium, the latter being arranged without regularity in the form of alveoli, cords, pegs, or nests; they are without glandular structure, and they show no regular central caliber. Cancer as a primary tumor exhibits the following varieties:

(a) In the variety termed *scirrhus*, or *hard cancer*, the connective tissue is comparatively abundant and well developed, either of loose, fibrous structure or compact, almost homogeneous. The epithelia are small, and arranged in narrow alveoli or in tracts, irregularly distributed throughout the connective tissue. (See Fig. 221.)

The connective tissue is fully developed, but scantily supplied with blood-vessels. The small, polyhedral epithelia are separated from each other by light, narrow rims of cement-substance, but interconnected by conical filaments, in the same way as normal epithelia. The epithelia are clustered together in small, irregular masses, and between the clusters and the adjacent connective tissue, in preserved specimens, a narrow space is

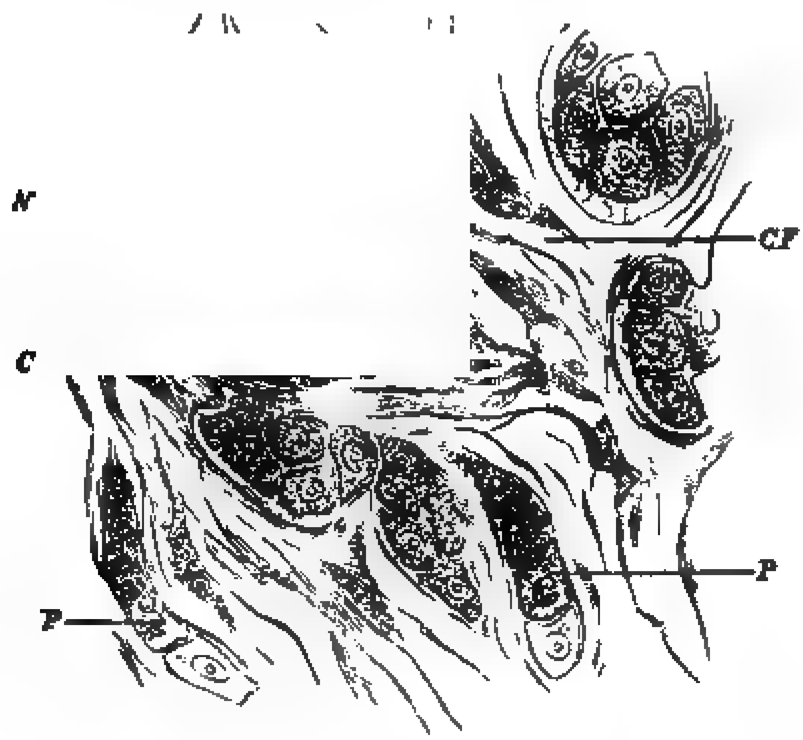


FIG. 221.—SCIRRHUS, OR HARD CANCER OF THE FEMALE BREAST.

N, alveolus, filled with epithelia. *CF*, connective-tissue frame, with *(CC)* clusters of plastids, the connective-tissue corpuscles; *PP*, rows of epithelia, probably sprung from connective tissue. Magnified 600 diameters.

often observed, containing granular matter or mucous globules, which are considered to be the offspring of endothelia, lining the inner surface of the connective-tissue cavity.

This variety is the least malignant and the slowest in its growth. It appears most frequently as a primary tumor in the female breast, at the side of the nipple, often retracting the nipple and producing folds in the skin. The comparativ

density of its structure, an occasional darting, lancinating pain, especially at night, are its characteristic features.

This tumor may exist for eight or ten years without any rapid increase in size, and without producing much discomfort to the patient. But after a certain time, almost invariably, the growth becomes more rapid, the pain more intense, and these changes mark the transformation of the tumor into medullary cancer, with a rapid unfavorable course and termination.

(b) In the variety called *epithelioma*, the epithelia are found lying in the connective-tissue frame as solid pegs or tracts or nests, in the centers of which a concentric arrangement is observed. The most central portions of the epithelia often undergo fatty degeneration, and produce shining, irregular masses of fat, the so-called cancer-pearls. The connective tissue is either of the myxomatous or fibrous variety, supplied with a moderate amount of blood-vessels, and either exhibiting fully developed basis-substance or a varying number of medullary or inflammatory corpuscles, replacing the basis-substance. (See Fig. 222.)

This tumor is of common occurrence in the skin and the mucous membranes. Some of its varieties are comparatively slightly malignant; for instance, the so-called *flat cancer* (rodent ulcer) of the skin of the face, whose cancerous nature was recognized thirty-five years ago by F. Schuh. The flat cancer produces shallow ulcers, without marked vegetations; the ulcer gradually penetrates into the depth of the tissues, and destroys them, including cartilage and bone. Though, owing to the presence of the small epithelial nests, the cancerous nature of this tumor cannot be doubted, it never produces secondary tumors in internal organs, but after a number of years kills by exhaustion.

The *nodular form* of epithelioma is most frequently observed on the lips, the tongue, the anus, the external genitals, and the vaginal portion of the uterus. It is rarer in the skin of the extremities, the mucosa of the larynx, and the œsophagus.

Sometimes the *papillary (cauliflower) character* of the epithelioma is marked, especially in the skin of the face, at the vaginal portion of the uterus, and in the mucosa of the bladder. As before mentioned, it is highly probable that such so-called papillary cancers have started as papilloma, and have gradually changed into cancer. None of the sub-varieties of epithelioma, though easily infecting the neighboring lymph-ganglia, are particularly prone to produce secondary tumors in internal organs.

(c) The variety called *medullary cancer* is the most malignant. It shows the following features:

The epithelia are very large and irregular in shape; sometimes they are of a polyhedral form and partly nucleated, sometimes homogeneous and shining. They exhibit endogenous multiplication in the shape of so-called mother cells, and also multiplication effected through wedges which spring from the living matter

P

E

N

C

FIG. 222.—EPITHELIOMA OF THE PREPUCE.

E, epithelial pegs; *N*, epithelial nests, with a concentric arrangement of the epithelia in the centers of the pegs and nests; *P*, so-called cancer-pearl in the center of the nests and pegs. *C*, connective tissue, crowded with medullary or inflammatory corpuscles. Magnified 200 diameters.

in the cement-substance. The connective tissue is scanty; it is fibrous in character, and incloses large and small groups of epithelia in closed alveoli. (See Fig. 223.)

The characteristic feature of what we call medullary cancer

is, therefore, the large number of epithelial formations in comparison with the connective tissue, the coarse granulation of the epithelia giving them the appearance of bright, homogeneous lumps — *i. e.*, solid masses of living matter, indicating an active morbid growth of epithelia. The compact lumps of bioplasson often appear as medullary corpuscles; the more rapid the growth of the tumor, the greater is the increase of the corpuscles and the more malignant the type of the growth. In the worst tumors of this kind, we can barely trace under the microscope fully developed, nucleated, polyhedral epithelia, arranged in nests; the main mass of the tissue is constructed of elements closely

FIG. 223.—MEDULLARY CANCER OF THE PAROTID GLAND.

E, regularly developed, polyhedral, nucleated epithelia, which at *H*, by increase of their living matter, have become shining and homogeneous; *M*, medullary corpuscles in a space inclosed by living matter (so-called mother-cell); *L*, vacuolation of epithelia; *F*, scanty connective-tissue frame. Magnified 600 diameters.

crowded together, exhibiting all the features of medullary corpuscles, and rendering the tumor a myeloma rather than a cancer. Transition of cancer into myeloma under these circumstances is often observed. An originally well-developed scirrhus may gradually assume the character of a medullary cancer, and this the features of myeloma. In the clinical variety of carcinoma

termed *lenticular cancer* (cancer en cuirasse, Velpeau), which starts from a cancer nodule of the breast, and in a comparatively short time invades all the soft tissues of the pectoral wall, the shoulders, the upper extremities, we look in vain for the epithelial cancer-nests, the main bulk of the tumor being constructed like a very malignant globo-myeloma. Secondary tumors in internal organs, chiefly the lungs and the liver, often exhibit no distinct epithelial nests, but only the structure of globo-myeloma.

Medullary cancer may appear primarily in any organ or tissue of the body, although unquestionably, in the majority of cases, it starts from organs which contain epithelial formations as anatomical constituents, and are, therefore, glandular.

The localities where primary cancer most frequently develops are: the female breast, the cervical portion of the uterus, and the stomach. According to Virchow the order in which the organs are invaded by *malignant growth in general* is the following: Stomach in 34.9 per cent.; uterus, vagina, etc., in 18.5 per cent.; large intestine and rectum in 8.1 per cent.; liver in 7.5 per cent.; face, lips in 4.9 per cent.; female breast in 4.3 per cent. of the cases; the sum total being 78.2 per cent. of fatal cases caused by malignant tumors.

The classification of cancers is, as here shown, a simple matter, but some pathologists are anxious to construct a large number of species and sub-varieties of cancer, with corresponding Greek and Latin denominations. The term "plexiform" is suitable for the designation of epithelial tracts branching and connecting within the connective tissue. It may be stated as a general rule that the larger the amount of connective tissue in a certain bulk of the tumor, and the smaller the number of epithelial nests, the harder will be its consistency and the less its malignancy. On the contrary, the smaller the amount of connective tissue, the larger the number of epithelial nests, the greater will be its malignancy. Myxomatous connective tissue between the epithelial nests necessarily lessens the consistency of the tumor without increasing its malignancy.

An important point for the determination of the degree of the malignancy of cancer is the presence of small, shining, globular elements in the connective tissue. Larger numbers of these formations invariably indicate a rapid growth of the tumor, and if occurring in a very large number they render the tumor a myeloma. This condition is only found in the worst types of

medullary cancer. The pathological significance of these elements differs according to the views of different authors. Those who believe the cancer epithelia to be an offspring of physiological epithelia, and consider them to have a certain specificity and independence of connective tissue (Thiersch, Billroth, Waldeyer, and others), assume that the medullary corpuscles in the cancer frame are due to an inflammation reactive upon the growth of the epithelia. While Virchow, who maintains a formation of cancer epithelia from connective tissue, considers these corpuscles as products of the "connective-tissue cells." The following article treats this subject more in detail.

THE ORIGIN OF THE CARCINOMA ELEMENTS. BY E. W. HOEBER, M. D., NEW-YORK.*

Regarding the origin of the cancer elements, pathologists nowadays hold two essentially different views. Virchow first announced that "connective-tissue corpuscles" might change into epithelial bodies; while Thiersch, Waldeyer, and others maintained the view that epithelium is endowed with the property of an independent development; epithelia of pathological formation, therefore, must always be the offspring of normal epithelia. The followers of the latter view seek support in the history of development, and avail themselves of the theory of the germinal layers, as established by Remak, for the explanation of pathological occurrences. To-day, arguments of this kind are of little value. The assertions of the independent action of the germinal layers fall to the ground in face of the fact that, before the appearance of such layers, the germ is entirely composed of elements destitute of any peculiar character, and it is not till later that special formations arise from these elements.

We know that in inflammation the tissue returns to a juvenile condition, and breaks down into the elements from which it had sprung. Elements produce their own kind only when in the embryonal condition. All observers, notwithstanding our limited knowledge as to the cause of the growth of tumors, are agreed that the parent tissue, in which a primary new formation originates, also returns to a juvenile stage or stage of indifference, in which it is capable of producing new elements. These, in further development, give rise to the characteristic tissue forms, which are mainly of two kinds : vascularized connective tissue and a vascular epithelium. It has been maintained that the epithelia are always offsprings of the upper and under germinal layer, while endothelia originate from the middle germinal layer, especially from the connective tissue. But even this apparently sharp distinction between epithelia and endothelia will lose its point if we take into consideration the fact that both epithelia and connective tissue originate from elements which are morphologically identical.

Köster has attempted to explain the development of cancers from endo-

*Abstract of the author's essay, "Ueber die erste Entwicklung der Krebselemente." Sitzungsber. d. Kais. Akademie d. Wissensch., 1875.

thelia of the lymph-vessels, without, however, throwing light upon this question. Recently, also, A. Classen has endeavored to include the "migrating cells" in the production of cancer, forgetting, evidently, the fact that "migrating cells" are always elements in the stage of indifference; that epithelia, if fully developed, are not possessed of the capacity of migration, and that no proof has yet been furnished of a new formation of tissue from wandering corpuscles.

The subjects of my researches were cancers which had been removed from the right parotid region, from the skin of the face, from the female breast, and from the liver. The characteristic feature common to all cancers is the

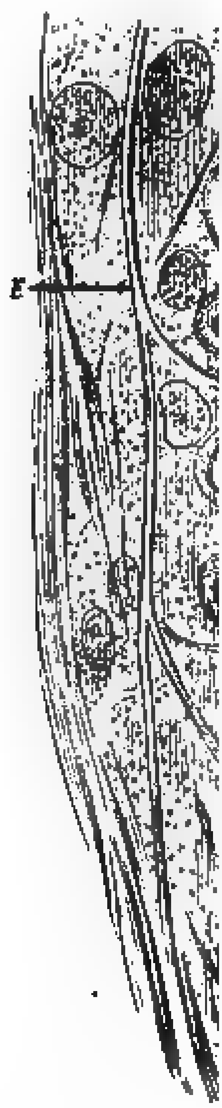


Fig. 224.—Cancer of the Skin of the Parotid Region.

CE, large, nucleated cancer epithelia, partly separated from each other by elastic fibers. *E*; *C*, unchanged fibrous connective tissue of the derma of the skin. Magnified 800 diameters.

epithelial new formation, the epithelial bodies, however, varying greatly in size. The largest I saw were in the cancer of the parotid region. (See Fig. 224.)

The cancer epithelia represented polygonal bodies, separated from each other by narrow rims of cement-substance having a ledge-like appearance and traversed by delicate spokes. Sometimes I saw the peg-like or alveolar for-

mations, filled with a continuous layer of bioplasson, with nuclei imbedded at regular intervals. In such layers — analogous to the so-called myeloplaxes — the cement-substance was partly or totally absent. A striking feature was that, in tumors of slow growth, the epithelia were small and their granules and lumps of bioplasson minute; while in cancers of rapid growth the epithelia contained coarse granules and large nucleoli. In the cancer of the liver, which had increased rather rapidly, the epithelia exhibited a very coarse granulation, and both within and between them were seen numerous lumps of a homogeneous appearance, without a reticular structure. Many of these lumps in the alveoli had no similarity whatever with true epithelial bodies.

The second constituent part of the cancer tumors — *i. e.*, the connective tissue — especially in those of comparatively rapid growth, exhibited the so-called "small cellular infiltration." (See Fig. 225.)

FIG. 225.— CANCER OF THE SKIN OF THE PAROTID REGION.

A, alveolus filled with epithelia. *L*, so-called "small cellular" infiltration of the connective tissue. *E*, formations within the connective tissue resembling epithelia. *V*, blood-vessel in transverse section. Magnified 800 diameters.

Examination with the highest powers of the microscope proved that this infiltration consisted of an accumulation of bright, globular homogeneous lumps, on an average not reaching the size of red blood-corpuscles. Each lump was almost constantly surrounded by a layer of bioplasson, whose granules were connected with the lumps by means of radiating filaments. The lumps assumed a violet stain after treatment with chloride of gold. They exhibited all phases of development, from compact masses to those which were pierced with vacuoles, and finally to those showing nuclei, which were inclosed by a thin shell and contained one or two nucleoli. Evidently these were bioplasson

formations in a stage of indifference, furnishing the material for specific formations.

Now, what is the source of these bodies? We observe that they appear first in rhomboidal fields, corresponding with the territories of connective tissue. At first one or two lumps only are visible in a territory; later the whole territory is transformed into a coarsely granular bioplasson mass, which contains a varying number of globular formations. In a still more advanced stage the territory is composed of polygonal plastids. Sometimes we see the connective tissue between two alveoli filled with flat elements, some of which contain large nucleoli. In such places it is apparent that a morphological difference

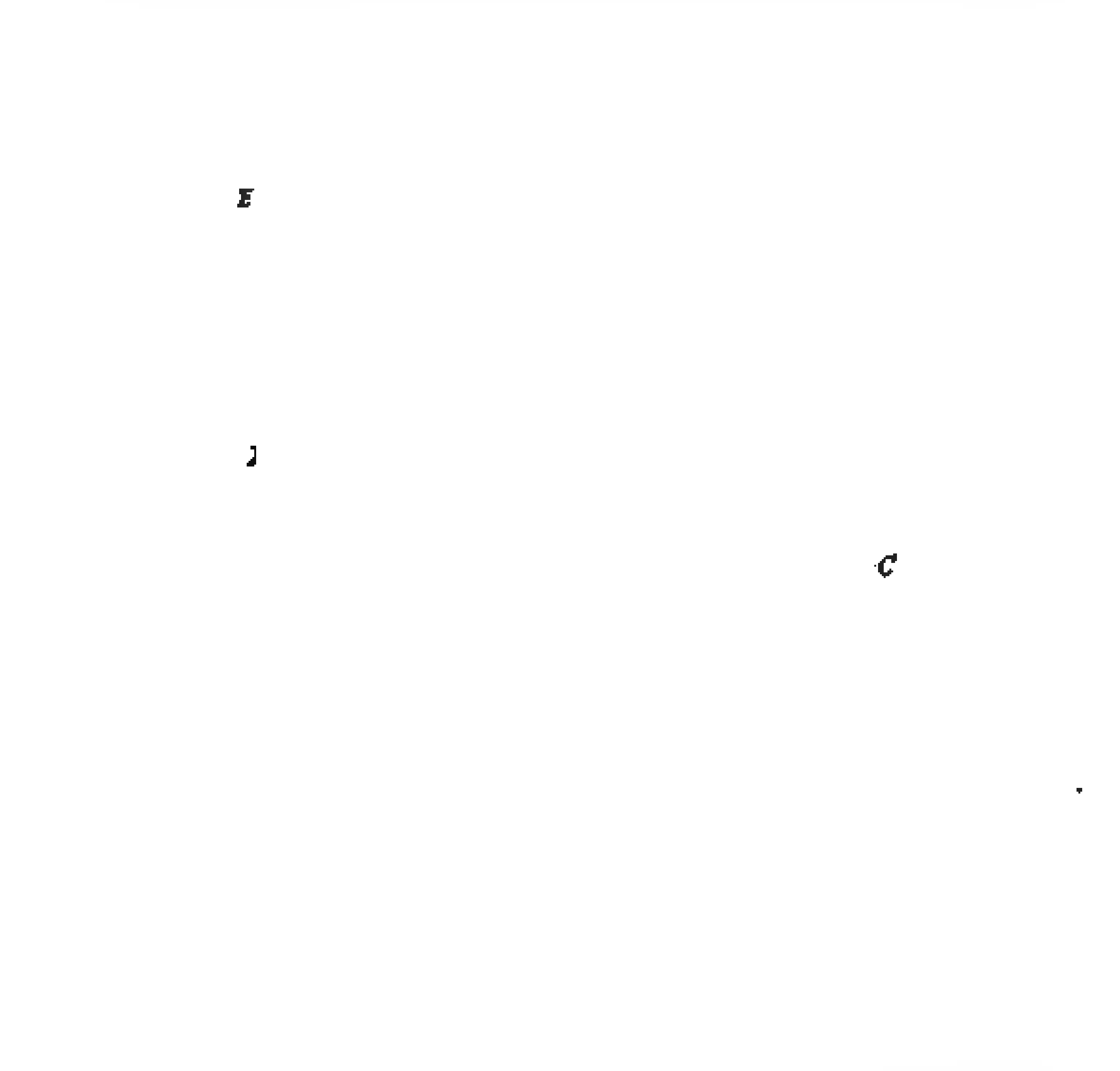


FIG. 226.—CANCER OF THE SKIN OF THE PAROTID REGION.

C, connective tissue; *EE*, epithelia, either arranged in closed alveoli or lying in the interalveolar connective tissue. Magnified 600 diameters.

does not exist between the elements occupying the alveoli and those which lie without much regularity in the neighboring connective tissue. (See Fig. 226.)

In specimens from a so-called flat cancer of the skin of the face, I observed that the connective tissue of the papillæ in some places was almost completely transformed into elements having the appearance of epithelia, and to such

an extent had this change progressed that only a delicate layer of fibrous connective tissue was left around the considerably dilated blood-vessels.

Sometimes we see in the connective tissue, besides the regular alveolar formations, spindle-shaped groups composed of small epithelial elements; many of these groups prove to be on all sides inclosed by connective tissue. Furthermore, epithelial formations occur which are traversed by a branching, shining, elastic reticulum, as illustrated in Fig. 224. The elastic fibers are arranged in such a way that the boundaries of the former territories of connective tissue still remain recognizable, while in some places the elastic reticulum replaces the epithelial cement-substance.

Finally, I would draw attention to rather common formations of the transition of indifferent bioplasson masses into distinct epithelial bodies. On the

FIG. 227.—CANCER OF THE LIVER.

L, bioplasson lump in the middle of a rhomb of basis-substance of connective tissue (Glisson's capsule); *R*, multinuclear, rhomboidal bioplasson formations, sprung from connective tissue; *V*, blood-vessel. Magnified 600 diameters.

one hand, small groups of a spindle- or rhomb-shape, composed of epithelia, are imbedded in the fibrous connective tissue bordering the large alveoli. (See Fig. 227.) On the other hand, the epithelial character of single elements in rapidly growing cancers is not marked, as before mentioned.

From what I have seen, I cannot support the decided distinction hitherto defined between epithelium and connective tissue. In the development of connective tissue we often observe formations bearing all the features of epi-

thelia—f. i., the so-called osteoblasts, arising from medullary elements. In both the epithelial and connective-tissue formations, in certain stages of their development, we meet with multinuclear bioplasson masses, in which in later stages either cement-substance or basis-substance makes its appearance. So far as the origin of different tissue forms is concerned, there is indeed a marked similarity between them all.

I maintain that in development of carcinoma epithelial formations appear in the connective tissue which are independent of former glandular formations. The proofs for this assertion are the closed spindle-shaped spaces of the connective tissue, which contain epithelia, and the epithelial formations which are traversed by branching elastic fibers.

The closed spaces of the connective tissue were supposed to be lymph-spaces, the endothelium of which had been transformed into cancer elements, or lymph-spaces into which cancer elements had immigrated. The first mentioned concept of authors I need not contradict, for the endothelium is admitted to be a formation of connective tissue. The second assertion lacks foundation, for epithelia themselves do not migrate, and the assumption of a transformation of indifferent migrating corpuscles into cancer epithelia does not assist us in the explanation of the origin of cancer.

My second proof is, I think, a still stronger one. It is that elastic fibers have never been observed in epithelial tissue, and, where they are present, they prove rather the origin of the epithelia from former connective tissue, whose territories are often bounded by elastic substance.

I, therefore, consider the epithelial formations in the midst of connective tissue as the result of a rejuvenescence of the latter, such as we observe in the inflammatory process. Under anomalous conditions the connective tissue returns to its medullary stage, which in sarcomatous growths remains stationary. If, on the contrary, the development from the medullary stage proceeds to the production of cement-substance, the medullary corpuscles assume the character of epithelia. The blood-vessels and their districts of nutrition may also have an influence on this process of development of epithelia, though the influence cannot be determined by observation, any more than an explanation is possible where the infection of cancer is located, which is transportable to neighboring lymphatics and to different and remote organs.

Virchow's assertion that in certain conditions epithelium arises from connective tissue I consider to be correct, and I would widen this assertion by adding that it is not the connective-tissue corpuscles alone which furnish new elements, but it is the totality of living matter contained in the basis-substance which participates in the production of new epithelial elements.

Local Origin and Transmission. Malignant tumors frequently arise from long-continued irritation or from traumatic inflammation. Cancerous tumors, especially, can be traced to such a source. After a number of years warts on the face, owing, perhaps, to some slight injuries inflicted in washing, may ulcerate and assume the character of cancer. In smokers, cancer of the lips is often produced by the long-continued friction of jagged, bitten pipe-stems. Cancer of the tongue often arises from ulcers pro-

duced by the friction of decayed and broken teeth; also from gummy tumors (Langenbeck). Persons addicted to alcoholic drinking are more prone to carcinoma of the œsophagus and stomach than those of temperate habits. Men in advanced age with a phimotic prepuce are subject to cancer of the penis; and those suffering from piles may acquire cancer of the rectum. Cancer of the breast and the uterus, in many instances, can be traced back to mechanical injuries. Ulcers of the skin, more especially the so-called varicose ulcers,—nay, simple callosities on the feet,—may take on a cancerous character. The primary cause for the growth of cancer we do not know. Middle and advanced age are most favorable for the growth of cancer—so much so, that it is rarely observed under the thirtieth year; it very seldom occurs in children. The older a person, the more liable is he to cancer. This disease is observed only in civilized races; travelers report it is never found amongst savages. A comparatively good constitution is requisite for its growth; individuals of the so-called phthisical constitution, or those broken down by chronic diseases, including syphilis, are not prone to cancer, though a gummy tumor may exceptionally give rise to a cancerous growth. Cancer and tuberculosis do not exclude each other, as was thought to be the case by older pathologists. In many instances we can trace the cancer as the primary disease, which, by breaking down the constitution, causes tuberculosis of different organs. I have observed eight cases of this kind.

Besides the local spreading of cancer, it almost invariably invades the lymphatics within its range, which are also transformed into cancer-tissue, and from which evidently starts the general infection. Secondary cancer formations have been observed not only in the lungs, the liver, or any organ, but sometimes almost all the internal viscera are found crowded with small nodules, identical in every respect to miliary tubercles, the so-called "miliary carcinosis."

The Development of Carcinoma in Lymph-ganglia.
By A. W. Johnstone, Danville, Ky.*

During the winter of 1880–1, whilst working in Dr. Heitzmann's laboratory in New-York, I examined four lymph-ganglia, three of which showed the initial stages of the formation of cancer.

The first came from a man, forty-eight years old, who had noticed a few small nodules on his prepuce. One of these was cut out and sent to the laboratory for diagnosis. Upon its being pronounced cancer the penis was

* Printed in abstract from the author's manuscript.

amputated. Six months later, two enlarged lymph-ganglia were found in the right groin; one as large as a hazel-nut, the other the size of a pea. Both were extirpated, and, although two years had since elapsed, the patient was perfectly well. The second ganglion came from a male inmate of Charity Hospital, New-York City, aged forty-two. He had a cancer of the throat that bled so freely that it necessitated the ligation of the right carotid. This was followed by excision of the tumor and the removal of an enlarged lymph-ganglion from the posterior maxillary region. The man died shortly after the operation, and at the post-mortem several abscesses were found in the lungs, and yellowish nodules in the liver and kidneys, which the microscope showed to be secondary cancer in its earliest stage of development. A male of over fifty years furnished the third specimen. About a year before, he was operated on for cancer of the skin on the leg. Shortly after, a number of new tumors arose, and the lymphatics of the groin began to swell. These new growths, as well as the lymphatics, were removed and brought to the laboratory. The fourth case was a woman of unknown age, who was operated on, in 1875, at the German Hospital of New-York City. A few indurated lymph-ganglia were removed from the axilla. The last specimen I removed from the foot of a lady. No enlarged glands were found, and she is now perfectly well.

The first three of these specimens contained all the stages of invasion, for they not only showed the fully formed cancer-tissue, but also the perfectly healthy adenoid structure. The fourth was composed of completed cancer-tissue.

The transmission of cancer from a primary focus to the adjacent lymph-ganglia is probably done by a transmission of its epithelia through the lymph-vessels. This, we know, is sometimes done; for in case (1) I saw a few epithelia scattered among the lymph-corpuscles of the cortical substance. Their size and shape distinguished them from all surrounding formations. Of course, this fact will not support us in denying that the fluid portion of the lymph coming from the cancer — the so-called cancer juice — may also transmit the infection. We are sure only that cancer epithelia are lodged in the lymphatic ganglia; but we are equally certain that we cannot explain why they or the juice can transform normal structures into cancer.

In the first three specimens I could trace, step by step, the whole of the cancerous metamorphosis. The first stage I found in that part of the ganglion where fibrous trabeculæ separated the healthy from the diseased tissue. This consisted of a melting down or running together of the elements and the formation of large multinuclear masses — the so-called myeloplaxes. I have not seen these formations in healthy adenoid tissue, but found a few small ones in a hypertrophied tonsil. There is no doubt that they spring from the confluence of the lymph-corpuscles in all their different stages of development, as well as from the myxomatous reticulum.

In the lymph follicle the corpuscles are connected with each other by delicate offshoots of living matter, which pierce the separating layer of liquid.

We may infer that all that is necessary to the formation of a "myeloplax" is the fusion of the jelly-like intertrabecular substance. The process of confluence of formerly separated corpuscles is shown in the earliest stages of a growing cancer, and in the invasion of a lymph-ganglion its central portion is generally first involved. Frequently I found an interfollicular string completely transformed into a continuous bioplasson mass, but still retaining its original shape. These masses are supplied at regular intervals with large

globular or oblong nuclei, which evidently are newly formed and have nothing to do with the original nuclei of the lymph-corpuscles. I have shown (see page 108, Fig. 31) that the myxomatous reticulum holds a delicate net-work of living matter, which, by the liquefaction of the basis-substance held in its meshes, becomes freed. This, most probably, is the process through which the myxomatous frame-work is converted into the same mass as the corpuscles. These masses are coarsely granular, which means that they are freely supplied with living matter.

The next stage is the appearance of cement-substance in the shape of straight, light lines, arising first in the middle of the bioplasson between the nuclei. At first, the cement-lines are scarce and in many places traversed by broad bridges of bioplasson. Later, the cement-substance assumes a regular polyhedral shape, though it is always pierced by delicate spokes of living matter, which are the inosculations of the reticula of living matter contained by the neighboring epithelia.

The last feature is the formation of a frame of connective tissue which divides the large bioplasson layer into smaller alveoli — the cancer nests. The first trace of this formation is the appearance of delicate nucleated spindles, which, by being split into smaller ones, build up the fibrous basis-substance. At the same time the blood-vessels of these trabeculæ are formed.

Not infrequently the cancer nests in the middle of lymph-ganglia exhibit concentric onion-like layers of epithelia, which in all probability arise from the pressure caused by the contraction of the surrounding connective tissue. In the center of a nest we often see epithelia undergoing fatty degeneration. Sometimes this has advanced to such an extent as to form a fat plug, which is always surrounded by flattened horny epithelia. I found this concentric arrangement in the first three cases. The fourth exhibited a fibrous frame inclosing irregular alveoli, filled with large and coarsely granular epithelia without any regularity.

The essential point in the invasion of lymph-ganglia by cancer is, first, the melting together of their components into large bioplasson masses. These in turn, by the formation of a cement-substance, are split up into polygons, which in groups become ensheathed by vascularized connective tissue, and thus give rise to the cancer nests.

The study of the last case, that of a rapidly growing primary cancer of the foot, forced me to the conclusion that the same changes take place in the formation of cancers in general. For along the edge of the fully formed carcinomatous tissue I found all the changes that I have just described. In this specimen, the infiltration of the normal tissues with globular corpuscles was unusually well marked. No doubt, the infiltration is itself a part of the cancerous metamorphosis, and it is only one of the steps of the adult tissue toward a complete transformation into cancer tissue. So far as the microscope can prove, this infiltration in its histological appearance is identical with adenoid tissue, and the globular corpuscles are identical with the lymph-corpuscles. In their retrograde change there is but one step toward the formation of multinuclear masses.

Secondary Changes of Cancer. Both the constituent tissues of cancer often undergo changes, which may either invade the

tumor in part only or throughout its entire mass. Among these changes I have observed the following:

(a) Fatty Metamorphosis of the Cancer Epithelia. This was known to the older pathologists as a yellow reticulum, usually seen in the central portions of the tumor. In the center of the nests in the variety termed epithelioma the epithelia are often transformed into fatty masses — the so-called cancer pearls. In scirrhus the fatty metamorphosis may invade a large number of epithelia, and in this way the tumor is robbed of its malignancy, at least to a certain extent. As a change subsequent to fatty metamorphosis, *calcareous deposition* occurs. This I found in a cancerous growth, the size of a pigeon's-egg, which I extirpated from the subcutaneous tissue of the lateral region of the neck; it exhibited calcareous depositions throughout all the epithelia to such a degree that it could be cut only after treatment with a chromic acid solution. Obviously, such a metamorphosis renders the tumor innocuous.

(b) Waxy Metamorphosis. This I have repeatedly observed in cancerous tumors. It transforms both the connective tissue and the epithelia into a shining, homogeneous mass, and, if combined with colloid degeneration, destroys the original structure, so that the latter is recognizable only in some portions which are less changed. Such a condition I have seen in a cancer of the parotid gland. Sometimes shining and concentrically striated — so-called amylaceous corpuscles — are present in the connective tissue frame, and these may also become the seat of calcareous deposition (the so-called arenoid corpuscles of Virchow).

(c) Colloid Metamorphosis. It occurs chiefly in cancerous tumors of the alimentary canal and the salivary glands, very rarely in external organs. This change very much lessens the malignancy of the tumor, although a recurrence has in some cases been observed after extirpation.

(d) Cystic Metamorphosis, which is closely allied to the colloid change. Both processes are considered in the following article.

(e) Pigmentary Metamorphosis. This is much rarer in carcinoma than in myeloma, and gives the tumor a brownish or bluish-black color to the naked eye. I have seen but one case of a tumor of this kind; it grew on the right shoulder of a man, and soon re-appeared after extirpation, which indicates that the presence of pigment increases the malignity of cancer, as it does that of myeloma. The recurrent tumor, in its uppermost portions,

exhibited the structure of cancer, with very large polyhedral epithelia and a comparatively scanty connective-tissue frame; both epithelia and connective tissue contained a large number of pigment clusters. The lower portion of the tumor showed the features of a pigmented myeloma, composed of large globular and spindle-shaped elements.

THE DEVELOPMENT OF COLLOID CANCER. BY H. G. BEYER, M. D.*

Epithelial formations exhibiting a central caliber, either acinous or tubular in shape, must be considered as adenomata; but such tumors, originally benign, are very prone to change into cancer and thus become malignant. When such a change occurs, the central caliber disappears, the connective tissue becomes infiltrated with shining globular elements, and epithelia are gradually developed therefrom.

It frequently happens that the original character of a carcinoma is, by secondary changes, partly or entirely lost. In fatty, waxy, or calcareous degenerations, the general configuration of the texture may be preserved. Other secondary changes, on the contrary, entirely destroy the original architecture of the tumor, leaving but few traces of its former primary character behind. Colloid, adenoid, and cystic cancer may be classified with this group. Colloid cancer is known to grow principally from the alimentary canal, the walls of the stomach, intestine, and rectum being its most frequent localities. Adenoid cancer is almost exclusively found in acinous glands, such as the lachrymal and salivary glands. Cystic cancer is only an exceptional occurrence in different parts of the body, but is met with most frequently in the ovaries. The specimen of this variety studied by me had formed in the liver, secondarily to medullary cancer of the stomach, and was, therefore, a great curiosity.

Of the colloid variety I had the opportunity of studying two cases: one from the stomach, the other from the large intestine. They are tumors of moderate consistence, infiltrating to a greater or less extent the walls of the stomach, respectively of the large intestine and the neighboring organs. The cut surfaces are of a pale grayish-yellow color, scantily supplied with blood-vessels, and upon being scraped with the knife yield a jelly-like, semi-translucent juice. In slight degrees of colloid change a precise discrimination between this and medullary cancer of moderate softness is not possible to the naked eye, while the high degrees of colloid degeneration, which lead to the formation of very soft, jelly-like, often granular, tumors resembling frog's spawn and quivering under the touch, are readily recognized.

The two cases of adenoid cancer which I have studied came from the submaxillary gland. To the naked eye the appearances were not very characteristic. Under the microscope they presented a coarse framework, composed of bundles of connective tissue bounding a number of closed alveoli, and holding a moderate quantity of blood-vessels. The smallest of the alveoli contained small but distinctly marked epithelia, while the larger ones held

* Extracted from the essay, "A Contribution to the History of the Development of Colloid Cancer." By H. G. Beyer, M. D., Assistant Surgeon, U. S. N.—*The Medical Gazette*, New-York, April, 1880.

peculiar star-shaped formations with a central nucleus-like body, from which a number of spokes were seen to emanate. These spokes, after traversing the alveolus, blended with its wall. The largest of the alveoli showed only traces of delicate branching fibrillæ, the main substance consisting, as in colloid cancer, of the so-called colloid mass.

Cystic cancer can easily be recognized by the naked eye. The tumor shows a number of sacs, the size of a pin's head to that of a walnut, holding a sero-albuminous fluid. Under the microscope, epithelial nests were found only at the periphery of the tumor. The cysts consisted of a wall of connective tissue, and in the serous liquid contained in their cavities only a few plastids were found.

Vertical sections obtained from the thickened wall of the stomach affected with cancer showed that the process of development had started from the submucous and muscle layers. A number of epithelial nests, bounded by smooth muscle-fibers, were found toward the periphery of the invading growth. In the neighborhood of epithelial formations the connective tissue had lost its fibrous structure and was transformed into finely granular bioplasson, within which large, shining, yellowish lumps were irregularly scattered. The bioplasson stage having thus been rëestablished, the change in the next consisted of an increase in size of the intersecting points of the living reticulum; these were transformed into medullary corpuscles, and, after having reached a certain size, became polyhedral by flattening each other, and in this manner were transformed into epithelia. The same characteristic changes took place in the smooth muscle-fibers. They were first transformed into rows of small, shining lumps of living matter, and passed by different stages of transition into epithelia. Groups of such epithelia were surrounded by newly formed connective tissue, the framework of the cancer.

In sections from the central portion of the tumor all the stages leading to a complete transformation into colloid cancer could be traced. Within the alveoli, bounded by newly formed connective tissue, a varying number of small medullary elements and a limited number of epithelia were observed; the remaining space was filled with a hyaline, apparently structureless, substance. Many of the alveoli were entirely devoid both of medullary elements and epithelia, holding only a homogeneous substance with remnants of living matter. Irregular clusters of epithelia could be seen here and there still attached to the cancer frame. Some of the connective-tissue bundles were in part coarsely granular and in part transformed into medullary corpuscles, giving rise to a myxomatous basis-substance. (See Fig. 228.)

In the most advanced stages of colloid change the field was traversed by a coarse, irregular reticulum of connective tissue, within which, besides a homogeneous substance, a more delicate fibrous net-work with remnants of epithelia were observed. Epithelia from these portions of the tumor, more especially when but one was present in an alveolus, had lost their polyhedral outlines, increased in size, as if by swelling, and had a globular or oblong shape. Some of them had increased three times their natural size, and presented the appearances of pale, dropsical, partly nucleated bodies.

In specimens obtained from the colloid cancer of the large intestine it was shown that the change had very uniformly invaded the entire tumor. Here large alveoli, separated by coarse bundles of connective tissue, could be seen, holding a very delicate fibrous reticulum, with isolated clusters of epithelia.

The reticulum within the alveoli was either irregular or, in certain places, arranged in a star-like manner. In the center was a cluster of plastids, sending out filamentous processes which blended with the wall of the alveolus. The spaces between the radiating threads were filled with a finely granular or homogeneous substance. In some alveoli, the reticulum presented an appearance identical with that of myxomatous tissue. In addition to these clusters of pale brownish-yellow epithelia, single, swelled, and dropsical-looking ones were also present, with pale granular contents. The latter evidently passed directly into the stage of myxomatous basis-substance. (See Fig. 229.)

Colloid cancer, consequently, is by no means a distinct species of cancer, but merely the result of secondary changes taking place in an originally medullary cancer. In the manner as cancer elements arise from medullary elements may fully formed epithelia, under certain unknown conditions, retrogress to medullary elements. Whenever this occurs, medullary corpuscles are transformed into a reticulum containing a jelly-like, homogeneous basis-substance, with interspersed remnants of epithelia. In the same manner, fully developed connective tissue may break down into medullary tissue,

FIG. 228.—COLLOID CANCER OF THE STOMACH.

F, connective-tissue frame. *E*, epithelia of cancer in the meshes of the connective tissue, *M*, medullary corpuscles sprung from epithelia, C^1, medullary corpuscles changing to colloid substance; C^2, alveolus filled with a homogeneous colloid substance, a few epithelia left unchanged. Magnified 500 diameters.

from which epithelia are developed, and epithelia may return to the medullary stage from which connective tissue is developed.

With these observations in the mind, the formation of the so-called adenoid cancer, too, can be readily understood. Here the alveoli originally contained cancer epithelia. These were changed into medullary corpuscles, from which were developed both the star-shaped myxomatous reticulum and the basis-substance filling its meshes. The center is occupied by either an unchanged epithelium or a cluster of medullary corpuscles, which have arisen therefrom.

Furthermore, we can understand the development of cystic cancer, the smaller cavities of which are also very often traversed by a myxomatous reticulum. The degenerative change of epithelia into myxomatous basis-substance reaches here its highest degree, and leads to the complete destruction of the myxomatous reticulum and to the liquefaction of its basis-substance.

Cysts are the results of a coalescence of alveoli, which is due to an augmentation of serous fluid accumulating in the alveoli, finally rupturing them. As regards their origin and development, there is no doubt about the identity of medullary, colloid, adenoid, and cystic cancer.

My investigations admit of the following conclusions:

1. *Whereas cancer epithelia are developed from medullary corpuscles, and also connective tissue and smooth muscle-fibers, under certain morbid conditions, break down into these corpuscles, cancer may develop indirectly from connective tissue and smooth muscle-fibers.*

2. *Cancer epithelia may return to the medullary stage and reproduce myxomatous connective tissue.*

3. *The reticulum of living matter, present in myxomatous connective tissue, is destroyed after the transformation of its basis-substance into colloid material.*

FIG. 229.—COLLOID CANCER OF THE LARGE INTESTINE.

F, connective-tissue frame, crowded with medullary corpuscles; *E*, epithelia of cancer, partly or entirely filling the alveoli, *M*, medullary elements, sprung from epithelia; *S*, cluster of medullary corpuscles, the center of radiating nucleated fibers, traversing the colloid substance. Magnified 500 diameters.

4. *Colloid and adenoid cancer originate from secondary changes of medullary cancer; the changes consisting, first, in the transformation of the contents of an alveolus into myxomatous basis-substance, next, in the further change of the latter into colloid substance.*

5. *Cystic cancer is but the result of a more advanced stage of liquefaction of the basis-substance of colloid cancer, accompanied by the formation of a connective-tissue sac—the wall of the cyst.*

XIV.

THE SKIN.

THE apparently complicated structure of the integument becomes easily understood, if we keep in mind that there are but two tissues entering the structure of the skin—viz., connective tissue and epithelium. The connective tissue produces the flat layer, called *derma;* the epithelium covers the derma on its outer surface. The boundary line between the two formations is not even, but fluted, supplied with numerous small protrusions of the derma, the so-called *papillæ*, the sum total of which bears the name "*papillary layer.*" The bundles of the connective tissue everywhere run an oblique course; they are arranged in the shape of a coarse reticulum in the lowest portion of the derma, whose rhomboidal meshes contain a varying amount of fat-globules, the so-called *subcutaneous tissue.* In the derma proper, the bundles run in two main directions, interlacing at acute angles, and thus producing a very dense felt, which by being tanned gives the leather. On the lowest portions of the derma the bundles are relatively coarse; they become finer nearer the papillary layer, and in the latter very delicate connective-tissue fibers are noticeable only, without a distinct arrangement into bundles. The epithelial formations on the top of the derma, again, exhibit two layers: the lower one, that nearest to the papillary layer, is living, and supplied with nerves, the so-called *rete mucosum;* while the outermost layer is composed of dry, horny epithelia, giving the formation called *epidermis.* The connective tissue is supplied with blood-vessels and lymphatics; the epithelium lacks such formations.

(1) *Subcutaneous Tissue.* The loose connective-tissue bundles, traversing the subcutaneous tissue, are prolongations of the subjacent membraneous formations, the fasciæ of the muscles, the aponeuroses, and the periosteum. The skin is firmly attached by means of short and coarse bundles, at the extensor surfaces of the articulations, in the groins, in the palms of the hands, and the soles of the feet. Here a varying number of single or multilocular spaces, containing a sero-mucous fluid, are usually found,—the so-called *bursæ mucosæ,*—which are inclosed by flat layers of fibrous connective tissue and lined with endothelia. In other localities, such as the eyelids, the upper portions of the auricle of the ear, the penis, and the scrotum, the attachment of the skin to the subjacent fasciæ is by loose, delicate connective tissue, containing no fat-globules. All other fibrous tracts of the subcutaneous tissue are more oblique in their course, and so extensible as to admit of a varying degree of pliability of the skin; they inclose rhomboidal spaces, which contain more or less numerous fat-globules. The latter are grouped in lobules, bounded by a delicate fibrous connective tissue, with a comparatively abundant vascular supply. This structure bears the name *panniculus adiposus.* (See Fig. 230.)

B

C

FIG. 230.—SUBCUTANEOUS FAT-TISSUE, THE FAT HAVING BEEN EXTRACTED BY TURPENTINE.

B, bundle of fibrous connective tissue, carrying injected blood-vessels; *C*, capsule of fat-globules, with oblong nuclei. Magnified 500 diameters.

(2) The *derma* or *cutis* is composed of dense interlacing bundles of fibrous connective tissue. Between the bundles we see a continuous branching bioplasson layer, with a varying number of nuclei, and sometimes with plastids, most of which are connected with the rest of the free bioplasson. The bundles appear very coarse in the lower, so-called reticular, portion, and are bounded by distinct elastic layers or elastic fibrillæ. These are less marked as the bundles become finer toward the papillæ, till in

the papillary layer they disappear altogether. The bundles of the derma have a certain regularity of arrangement, as is demonstrated by the researches of C. Langer. This investigator punctured the skin with a shoe-maker's awl, and after the withdrawal of the instrument observed, in every instance, instead of round holes, longitudinal clefts, regularly distributed over the entire surface of the body. There are a few places where the awl produces irregular jagged openings in the tissue of the derma; these are most marked in localities where the derma is closely attached to the subjacent tissues. The same investigator found that the striae of the skin of the abdomen and upper part of the thighs, produced by over-extension, usually in pregnancy, are caused by stretching in a horizontal direction of the bundles of the connective tissue of the derma. The blood-vessels also assume a horizontal course, following the stretched bundles. The epithelial cover remains unchanged.

In the derma, the connective tissue is mixed with a varying amount of *muscles*. The *striped variety* is seen in the skin of the face and the lateral aspect of the neck, where the lowest bundles connect with striped muscle-fibers, often in a reticular arrangement. In many animals the derma has an almost continuous layer of striped muscles, the so-called *panniculus carnosus*, which enables these animals to produce voluntary movements of the skin. Bundles of *smooth muscle-fibers* are scattered throughout the derma, either in a reticular or fan-like arrangement, or in the shape of single oblique bundles. The reticular arrangement of smooth muscle-bundles presents itself in the skin covering the nipple and its areole, the penis and the scrotum. In the skin of the penis the direction of the muscle-bundles is mostly circular, in the scrotum antero-posterior. The fan-like arrangement, and that in single bundles, occurs all over the skin, the muscles, so-called *arrectores pilorum*, being everywhere in close relation to the hair-follicles. According to W. Tomsa the connection between the smooth muscle-fibers and the tissue of the derma is established by elastic fibers, which are twined around the muscle-bundles. This relation is specially marked in the arrectores pilorum. The connective tissue ensheathing the larger coils of sweat-glands exhibits smooth muscle-fibers, which produce an almost continous layer around the sweat-glands of the axillæ.

The *papillary layer* — *i. e.*, the outermost portion of the derma —is composed of delicate fibers of connective tissue, not distinctly

interlacing, and freely supplied with small nuclei along the fibers. The boundary line toward the epithelium is slightly fringed, as seen where the papillary layer is withdrawn from the rete mucosum; sometimes a hyaline, so-called structureless, layer may be observed. (See Fig. 231.) The papillæ are prolongations of the derma, varying greatly in size and shape in different localities of the integument. The largest and most numerous papillæ, composed of a number of filiform elevations which coalesce into a more bulky basis, are found on the palmar surface of the hands and the plantar surface of the feet. In other places they form small conical or blunt protrusions. The papillæ are every-

L

T

FIG. 231.—PAPILLARY LAYER OF THE SKIN OF A CHILD. VERTICAL SECTION.

The papillæ are artificially separated from the covering epithelium. *E*, epidermis; *R*, rete mucosum; *C*, row of columnar epithelia nearest to the connective tissue; *P*, papillæ, composed of delicate fibrous connective tissue; *L*, longitudinal; *T*, transverse section of bundles. The blood-vessels injected. Magnified 500 diameters.

where arranged in rows, between which crossing furrows are present, visible to the naked eye, produced by a peculiar arrangement of the connective-tissue fibers, which is also marked on the outer epidermal surface. The rows formed by the groupings of the papillæ are especially well marked in the palms of the

hands and the soles of the feet, giving rise to the graceful spiral and concentric lines observed on the skin covering the last phalanges.

In horizontal sections of the skin the papillæ appear as light, circular, or oblong fields, marked by the presence of transverse or oblique sections of the capillary blood-vessels in their central parts. The depressions between the papillæ are filled with epithelia, which, being arranged in the form of an interpapillary reticulum, have given rise to the inappropriate name "rete mucosum." (See Fig. 232.)

According to J. Collins Warren,* the papillæ are imperfectly formed on the posterior aspect of the body. The follicles of the lanugo hairs penetrate the superficial layers of the derma, the sweep of whose fibers would be unbroken were it not for the existence of a structure which connects the bases of the hair follicles with the panniculus adiposus. This consists of a columnar cleft extending from the subcutaneous tissue in a somewhat oblique direction through the cutis to the base of the hair follicle. This cleft is filled with adipose tissue, hence the term "fat-column" is appropriate for its designation. Its long axis is placed at a slight angle to that of the follicle, and is nearly parallel to that of the arrector pili muscle. The number of fat-columns corresponds to the number of hairs. They are seen

FIG. 232.—SCALP OF A COLORED MAN. HORIZONTAL SECTION.

R, rete mucosum; *Pt*, row of columnar epithelia, cut obliquely, supplied with dark-brown pigment granules; *Pa*, papilla, cut transversely; *D*, derma. Magnified 500 diameters.

* "A Manual of Histology." By Thom. E. Satterthwaite, New-York, 1881.

most distinctly in the thickest portions of the skin, but may be also found on the shoulders and arms, the breast, abdomen, and the lower extremities, although sometimes only slightly indicated.

(3) *Blood-vessels.* The arteries, which supply the skin, penetrate the subjacent fasciæ and anastomose with each other above the fasciæ; they are more numerous in the flexor surfaces of the extremities than in the extensor, and than in the trunc. The largest number is found in the palmar and plantar surfaces. In accordance with the accurate researches of W. Tomsa, the skin everywhere has three separate vascular districts, each of which is supplied with its own arterioles and roots of veins. The deepest is that of the subcutaneous fat-tissue; the next in order is that of the sweat-glands, and the most superficial belongs to the derma, with its hair follicles and sebaceous glands. The arterioles which supply the fat-tissue are numerous, corresponding to the large number of capillaries; those of the sweat-glands surround the coils in a basket-like arrangement and empty into two or three veinlets, one of which invariably runs upward along the duct of the sweat-gland and anastomoses with veins of the papillary layer. The artery, after supplying the above-named formations, ascends to the papillary layer of the derma, and in its course branches into capillaries which go to the hair follicles, the sebaceous glands, and the papillæ. Before reaching the papillæ, the arteriole splits into precapillary ramules, from which arise the capillaries proper. These form loops which, as a rule, are single, but in the largest papillæ double, and unite into an extended flat reticulum of a venous character. In portions of the skin with large papillæ there is a double layer of veins, the superficial arranged in narrow and elongated meshes, the deeper, on the contrary, in wide and more circular ones. These vessels give rise to venous branches, uniting at acute angles into larger veins, which produce arches and receive the veins of the sweat-glands and the fat-lobules. The hair follicles have between the two layers of the follicle wide, transversely arranged capillaries, which penetrate its inner layer also. In the upper portion of the follicle numerous anastomoses exist with the capillaries of the papillary layer, and in this situation arise the capillary loops for the supply of the sebaceous glands. All these capillaries unite into an irregular venous net-work, which is lodged in the external layer of the hair follicle, and anastomoses freely with the venous vessels of the papillary layer. The papilla of the hair has

its own arteriole, which branches into looped capillaries, emptying into the common venous reticulum of the hair follicle. The vascular district of the papillary layer also furnishes the supply for the muscles, the ducts of the sweat-glands, and the larger nerves. The muscle-layer of the scrotum only has an independent vascular supply.

(4) *Lymph-vessels.* Successful injections of the lymphatics of the skin with colored liquids have proved that these vessels constitute a closed reticular system, in two layers, interconnected by oblique branches. The superficial layer of capillary lymphatics is situated in the papillary portion of the skin, beneath the superficial layer of blood-vessels. It is composed of ramules, closer and narrower than those of the deep layer; from it the larger papillæ receive blind offshoots or shallow loops. I. Neumann describes lymphatic reticula around the hair follicles, the sebaceous and the sweat glands. The wide lymphatic branches which spring from the deep layer are destitute of valves, and accompany the arteries producing capillaries twined around the arteries. After having received the lymphatics of the subcutaneous tissue they are furnished with valves, and take their course in this tissue in large numbers, especially in the flexor aspects of the extremities.

(5) *Nerves.* The skin is abundantly provided with both medullated and non-medullated nerve-fibers, more especially in the palms of the hands and the soles of the feet, particularly in the skin covering the last phalanges of the fingers and toes. The nerves usually penetrate the derma together with the blood-vessels. Some of the medullated nerve-fibers terminate in the subcutaneous tissue as Pacinian corpuscles; others reach the upper portions of the derma in bundles, where they produce a plexus. From this plexus arise branches for the nervous supply of the papillæ and the epithelial layer, some of which are medullated and some non-medullated. The medullated nerve-fibers run to the larger papillæ, which, as a rule, are destitute of blood-vessels, and terminate as a tactile corpuscle either in the papilla or at its base, or even below its level. (See Fig. 233.)

The corpuscles of Pacini or Vater are ovoid bodies, discernible to the naked eye, some of them attaining a longitudinal diameter of two mm. or more. According to Genersich, they increase in size with advancing age. They are attached to medullated nerve-fibers, and are composed of a number of concentric, nucleated layers, more closely arranged at the periphery of the corpuscle than toward its center, and freely supplied with capillary vessels

of their own. Hoyer discovered, by means of silver-staining, a system of dark brown lines, analogous to that in the endothelia. The medullated nerve-fiber enters the corpuscle at one pole, and gradually loses its myeline investment, while the myeline sheath is lost in the structure of the concentric lamellæ. The axis-cylinder terminates at the distal pole of the corpuscle as a simple knob, or it bifurcates into two branches, each of which may also exhibit a terminal knob. Around the axis-cylinder is found a granular layer with nuclei. Pacinian corpuscles are most numerous along the nerves of the fingers and toes, less numerous in the palmar and plantar surfaces and in the vicinity of larger articulations in the subcutaneous tissue of the nipple, penis, and clitoris, also along the branches of sympathetic nerves, more especially behind the pancreas, in the dura mater, the periosteum, etc.

The *tactile corpuscles* (Meissner's or Wagner's corpuscles) are ovoid bodies, rarely exceeding 200 M in length, and composed of

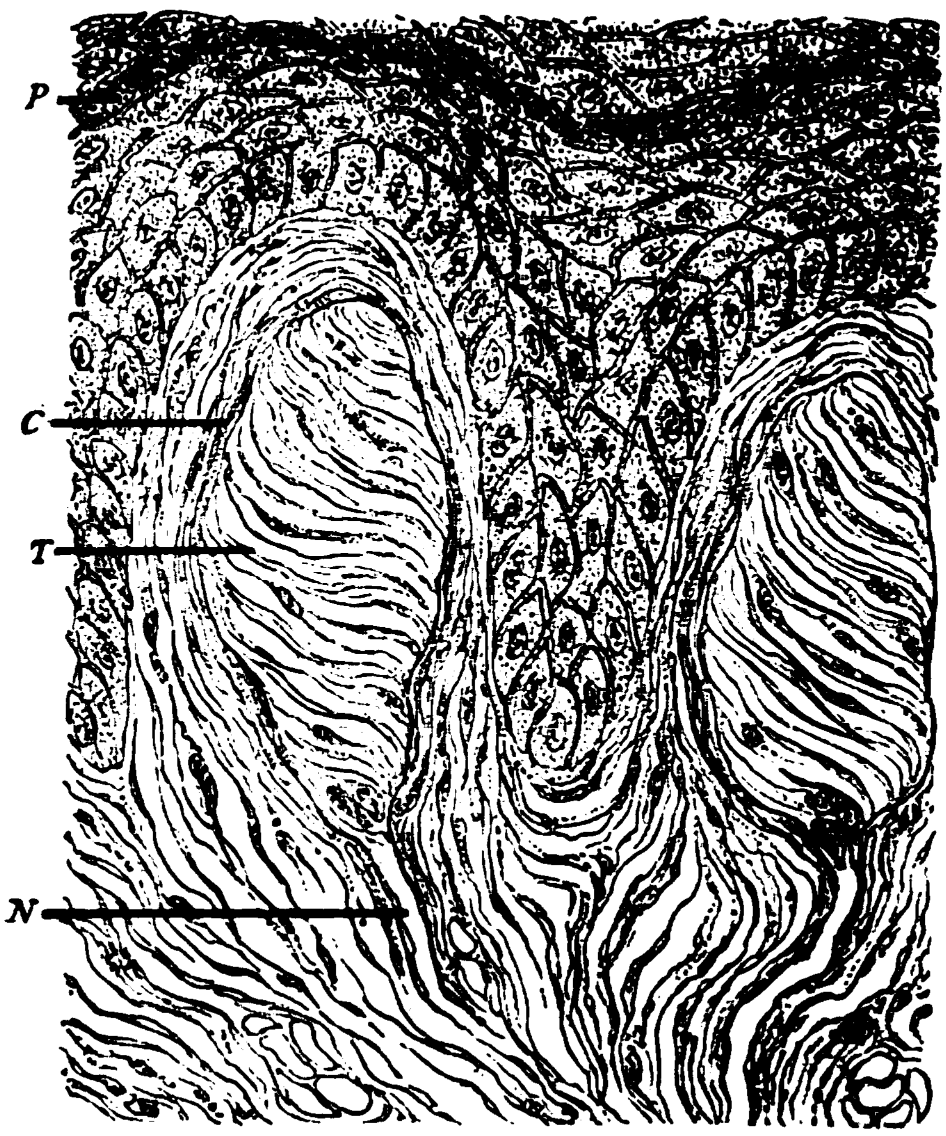


FIG. 233.—TACTILE CORPUSCLES IN THE PAPILLÆ OF THE SKIN OF THE FINGER-TIP.

N, medullated nerve-fiber; *T*, tactile corpuscle; *C*, connective-tissue sheath; *P*, pigment-layer of the rete mucosum. Magnified 500 diameters.

spiral fibers with small nuclei. Around them a somewhat denser connective-tissue capsule is seen. One or two medullated nerves enter the corpuscle at one pole, their myeline sheath being lost in the fibrous mass of the corpuscle. The axis-cylinder divides into a number of delicate fibrillæ, running with the spiral fibers;

their ultimate termination is not known. Sometimes the tactile corpuscle exhibits deep furrows, indicating that it is composed of several tactile buds (Merkel), or two or more isolated tactile corpuscles are attached to one or two nerves (Oehl, Thin, and others). A. R. Robinson * maintains that the nerve does not terminate in the tactile corpuscle, but passes on into the rete mucosum; the axis-cylinder generally changes the direction of its course after leaving the corpuscle, and terminates between the epithelia.

Non-medullated nerve fibers are known to terminate in the walls of the capillary blood-vessels of the papillary layer (Tomsa), and in the rete mucosum (Langerhans, Flemming). In the latter situation a delicate beaded reticulum of nerve fibrillæ can be brought to view, especially by staining with chloride of gold, but the question is unsettled whether or not the nerves enter the epithelia. Tomsa noticed a delicate reticulum of nerves around the coils of the sweat-glands; others have described such a reticulum in the follicle and the papillæ of the hair.

(6) *The Epithelial Cover of the Integument.* The outer layers of the stratified cutaneous epithelium are squamous, the middle, which are the most abundant, cubodial, and the boundary, toward the papillæ, consists of a single row of columnar epithelia. The columnar and cuboidal epithelia are endowed with vital properties, of which the flat epithelia are deprived by their transformation into a horny material. The living portion of the epithelium bears the name of *rete mucosum*, or *rete Malpighii*; the horny portion is the *epidermis* proper. Between these two layers appears a narrow zone of nearly compact glistening epithelia, running parallel with the surface; Oehl has designated this layer the *stratum lucidum.* It is sometimes well marked, especially in vertical sections of the skin covering the palms of the hands and soles of the feet; sometimes it is not discernible. At other times alternating layers are found, consisting of granular, nucleated, and of nearly homogeneous epithelia, destitute of nuclei; but as these formations are not constantly present, we are not justified in dividing, as some authors have done, the epithelial cover of the integument into four or five distinct layers.

The epithelia nearest the papillary layer are often indistinctly columnar, and of a diffuse brownish color, holding more

* "A Manual of Histology," by Thomas E. Satterthwaite. New-York, 1881.

or less pigment-granules. In the Caucasian race these are best observed in the region of the nipple of the breast, the external female genitals, the scrotum, and the anus. In the colored races (see Fig. 232) the columnar epithelia contain numerous blackish-brown pigment-granules, always scattered around the central nucleus, which itself remains uncolored. The pigment-granules, by means of delicate filaments, are connected with the bioplasson reticulum within the epithelia. Between the columnar, as well as the neighboring cuboidal epithelia, the cement-substance is invariably traversed by delicate transverse filaments, and contains a varying number of homogeneous or granular bioplasson bodies. These are growing epithelia, wedged between the older formations, and interconnected with them by delicate offshoots. Some authors have mistaken these lumps for connective tissue or wandering cells.

The epithelia of the rete mucosum are irregularly polyhedral, also supplied with a diffuse coloring matter, and distinctly nucleated. The cement-substance shows the connecting transverse filaments, especially after treatment with chloride of gold. The filaments (so-called thorns) are easily discernible in places which were subject to a slight, continuous irritation (see page 323, Fig. 139). The cement-substance in this situation likewise holds small, solid lumps of bioplasson, which are best marked and most numerous in the localities exhibiting the thorns most plainly. In the cement-substance of specimens successfully stained with chloride of gold we find the beaded axis-fibrillæ. Toward the periphery the cuboidal epithelia are slightly flattened and finely granular, which indicates that the epithelia are gradually dying, though the vitality is usually retained by the nucleus. There may be layers above the rete mucosum, composed of flat epithelia, either homogeneous or distinctly nucleated, and readily stained by carmine, which shows that they are endowed with a higher degree of vitality.

The most external portion is composed of flat, imbricated epithelia, which in the vertical section appear spindle-shaped. Their horny nature is demonstrated by an irregular contour, by the want of granulations, and by the absence of a nucleus. The nucleus may be found, however, in the lowest portions of the horny layer, though it is often only faintly indicated. The properties of life in these epithelia are gradually lost, and are entirely absent in the outermost, flattened epidermal scales. We know that the epidermal scales desquamate during life, but the

question how a new growth of epithelia goes on, replacing the lost epidermal scales, is as yet not quite settled. In persons of dark complexion the horny epithelia also exhibit a diffuse yellow-brown color.

(7) *Implantation of the Hairs.** If we imagine that the connective tissue, together with the covering epithelium, were a pliable sheet of chamois, for instance, and we produce a depression of this sheet with one of our fingers, the result will be a pouch, whose innermost layers are epithelial, whose outermost layer is connective tissue. The epidermis will cover the inner surface of the pouch, and now bear the name *inner root-sheath;* next to this will be a layer formed by the epithelia of the rete mucosum, which will be the *outer root-sheath;* the outside of the pouch must be connective tissue, and will represent the *follicle.* At the bottom of the pouch will be a protrusion of the follicle, similar to those on the surface of the skin, therefore connective tissue—the *papilla of the hair.*

On our diagram slight alterations must be made. The epidermis, which is composed of a large number of flat epithelia, varying greatly according to the width of this layer, upon entering the pouch and becoming the inner root-sheath, will gradually be reduced to a limited number of horny epithelia—in the middle of the pouch to not more than two strata. Near the bottom of the pouch the number of the epithelia again increases, the inner root-sheath gains in width, and is composed of three or four strata of epithelia which have lost their horny character, and assume again the nature of bioplasson. The rete mucosum enters the pouch in its full width, but gradually becomes thinner,—namely, composed of a smaller number of epithelia, which retain their original bioplasson character,—and at last, near the bottom of the pouch, after being reduced to a single layer, completely disappears.

Imagine, now, that against the bottom of the epithelial pouch, which runs in an oblique direction, corresponding with the disposition of the connective-tissue bundles, a pin is pressed and the pouch turned upward again. This procedure, of course, will involve the inner root-sheath exclusively, and an elongation must result of an epidermal character, agreeing with the main features of the inner root-sheath. This elongation represents the *hair.*

* "A Contribution to the Minute Anatomy of the Skin." Read before the American Dermatological Association, Newport, R. I., September 1, 1881. *The Chicago Medical Journal and Examiner*, December, 1881.

The hair, therefore, is a solid elongation of the hollow inner root-sheath, and produced by the inner root-sheath alone. The outer root-sheath has nothing to do with the formation of the hair. At the bottom of the pouch there is a knob composed of living epithelia, resembling those of the inner root-sheath in the same situation. This knob is called the *bulb of the root of the hair*, and directly surmounts the papilla of the hair. Higher up the epithelia again become horny, and enter into the construction of the *root* and the *shaft of the hair*.

Imagine, lastly, that, on the side of the acute angle of the obliquely implanted pouch, the outer root-sheath, which is, as

FIG. 234.—DIAGRAM OF THE IMPLANTATION OF THE HAIR.

E, epidermis; *RM*, rete mucosum, *PL*, papillary layer; *IS*, inner root-sheath, *OS*, outer root-sheath; *F*, follicle; *D*, derma; *M*, arrector pili muscle; *P*, papilla of the hair; *B*, bulb, *C*, cuticle; *R*, root; *S*, shaft of the hair, *SG*, sebaceous gland.

said before, an offshoot of the rete mucosum, be pushed laterally and downward by a pin, the result will be a third elongation, produced by the outer root-sheath, a small pouch itself, bearing the name *sebaceous gland*. According to this diagram, *the sebaceous gland is an exclusive formation of the outer root-sheath*, while the inner root-sheath takes no part in the formation of the gland. (See Fig. 234.)

The explanation of the diagram is as follows: The epidermis, bulging downward, results in the formation of the inner root-sheath, while the rete mucosum, prolonged downward, forms the outer root-sheath.

The bundles of the connective tissue of the derma, which give an outer investment to the pouch, composed of both root-sheaths, produce the follicle. Its innermost portion exhibits cross-sections of smooth muscle-fibers.

The papilla of the hair is a product of the follicle. Around the papilla is a knob — the bulb of the root of the hair — which continues into the *root of the hair* — that part inclosed in the pouch; and the *shaft of the hair* — that part standing forth on the surface of the skin.

The diagram shows that the inner root-sheath, upon approaching the bottom of the pouch, becomes widened, and at the bottom of the pouch turns over, thus first producing the bulb, afterward the root, and the shaft of the hair itself. The innermost layer of the inner root-sheath, by turning over, results in the formation of the cuticle, the single investing layer of both the root and the shaft of the hair.

The figure demonstrates, furthermore, that the outer root-sheath, upon approaching the bottom of the pouch, becomes thinner, and perishes at last, while on one side the outer root-sheath produces the pouch of the sebaceous gland. Between the outer root-sheath and the follicle there is a homogeneous layer — the so-called structureless membrane. The arrector pili muscle is in connection with the muscle-layer of the follicle and surrounds the bottom of the sebaceous gland.

Our diagram serves as a key, which enables us to comprehend easily all formations of the skin engaged in the construction of the hair. (See Fig. 235.) The pouch, as a rule, has a funnel-shaped widening on the surface of the skin, which is covered by stratified epidermal scales. These scales are traceable in direct union with the inner root-sheath, which begins on the so-called neck of the pouch, being composed of two epidermal layers only, and, in honor of the discoverer, termed Henle's sheath. Next to the inner root-sheath lies the extremely delicate cuticle of the hair, which ensheathes both the root and the shaft of the hair. With higher powers we see on each hair finely serrated edges — the slightly bulging edges of the cuticle. The hair is composed of closely packed, horny epidermal spindles, which hold a varying amount of pigment granules. The rete mucosum elongates directly into the outer root-sheath, and this into the sebaceous gland. It is only the duct of this gland which is covered by flat, horny epithelia, while the gland, as such, is composed of cuboidal epithelia, like any acinous gland. The duct of the sebaceous gland, as a rule, empties into the funnel-shaped widening of the pouch, in the space between the inner root-sheath and the hair, or, more particularly, its covering cuticle. The outer root-sheath is composed of several strata of epithelia, like the rete

mucosum itself. The strata are cuboidal epithelia, and it is only the layer nearest the derma, or, more properly, the structureless membrane, which is formed by columnar epithelium. The inner surface of the structureless membrane, again, is covered by

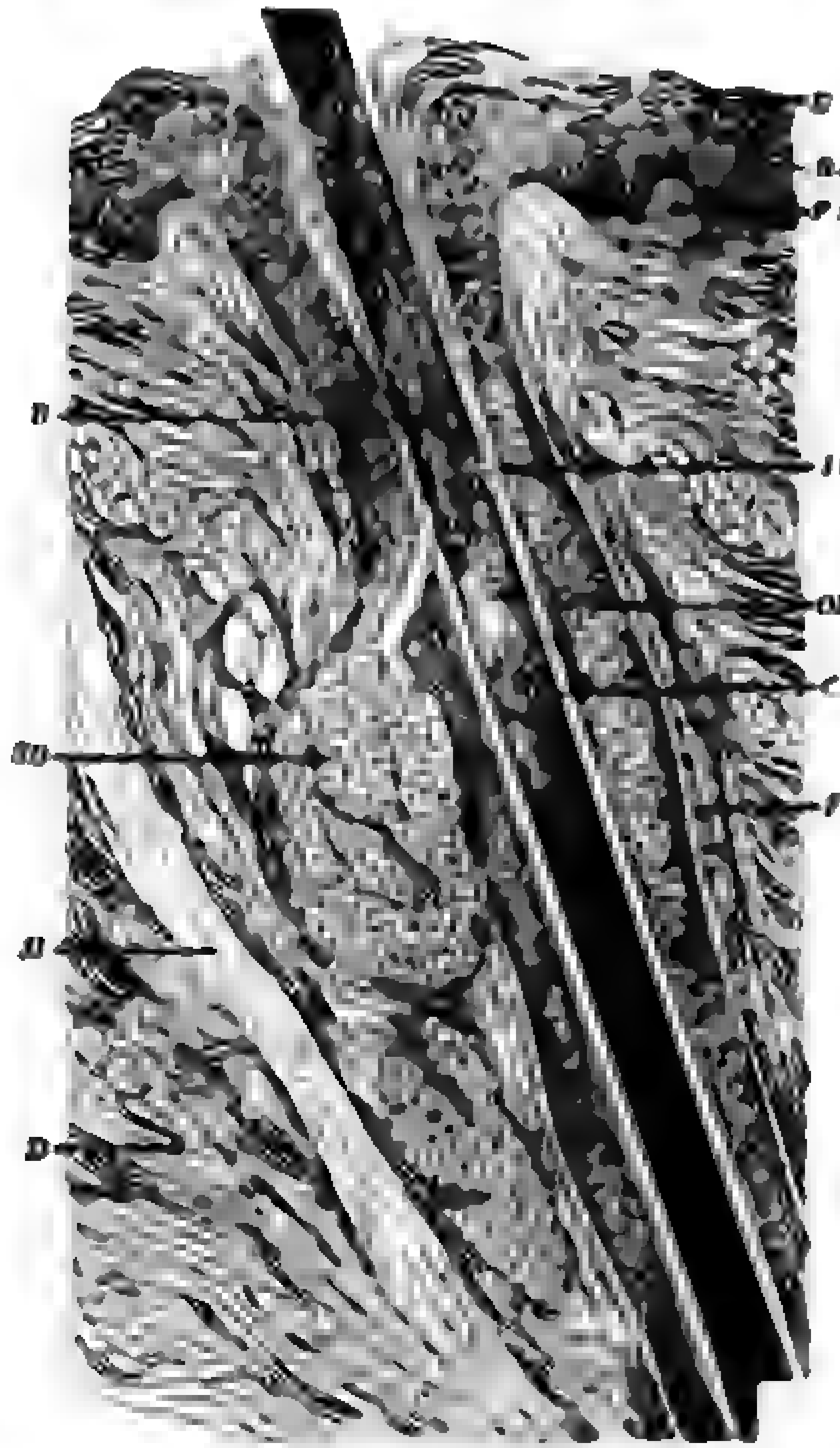


FIG. 236.—THE LOWER PORTION OF THE HAIR-FOLLICLE FROM THE HUMAN SKIN.

E, epidermis. R.M, rete mucosum. P.L, papillary layer. D, dermis. F, follicle. M, erector pili muscle. Sb, sebaceous gland. O.S, outer root-sheath. I.S, inner root-sheath. C, cuticle. S, shaft of hair. Magnified [illegible] diameters.

extremely delicate flat endothelia, as was first demonstrated by the aid of silver-staining by V. Czerny. These endothelia are

directly connected with the adjacent columnar epithelia by very marked prickles and thorns. To the presence of these thorns D. Haight first drew attention.

The pouch of the sebaceous gland is under the control of the *arrector pili muscle*, which represents a flat, fan-like sheet, whose broad ends terminate in the papillary layer, while the narrow end is inserted in the follicle of the root of the hair. No doubt, the evacuation of the sebaceous gland is done by contraction of this muscle-sheet. The fatty mass will be squeezed first into the funnel of the hair-pouch, as a rule, and only from large sebaceous glands directly to the surface.

The lower extremity of the hair-pouch, in specimens taken from the human skin, is readily understood if we have made a study of the hair of animals, especially of those strong hairs on the upper lip of kittens. It is, perhaps, for this reason that, after many years' busy writing, not one author has given a plain description of the relations. As a matter of course, the essentials are identical in the hair of kittens and that of man, though the former are, as a rule, plainer than the latter. (See Fig. 236.)

The inner root-sheath in its upper portion shows the light, horny Henle's layer. In an oblique line there appear polyhedral epithelia; in the upper portions pale and finely granular, with indistinct nuclei; deeper down, coarsely granular and slightly elongated. This latter part of the inner root-sheath represents what has been termed Huxley's layer. It is seen that at the bottom of the pouch this layer turns over, surrounds the papilla, and constitutes the bulb of the root of the hair. The epithelia on the lower periphery of the papilla are columnar, gradually changing into the cuboidal form, and farther up become elongated, spindle-shaped. Lastly, they emerge into the horny spindles which produce the main bulk of the hair. The boundary line between the inner root-sheath and the root of the hair is produced by a thin, apparently structureless, layer, outside of which is the inner root-sheath, inside the cuticle of the hair. The cuticle on the upper portion of the root is composed, as well as on the shaft, of thin, imbricated scales, whose edges are slightly elevated above the surface of the hair, and give the latter the peculiar serrated appearance. Gradually, the epithelia of the cuticle of the root assume a columnar shape and become nucleated. At the height of the bulb these columnar epithelia are very large, pale granular, and supplied with large and distinct nuclei. Their characteristic row runs in the middle, between Huxley's

layer and the bulb, and at last blends with the cuboidal epithelia of both formations. Outside of the cuticular row there is another thin layer of pale, flattened epithelia, which evidently corresponds to the innermost structureless layer of the inner root-sheath. The middle portion of the bulb is often filled with

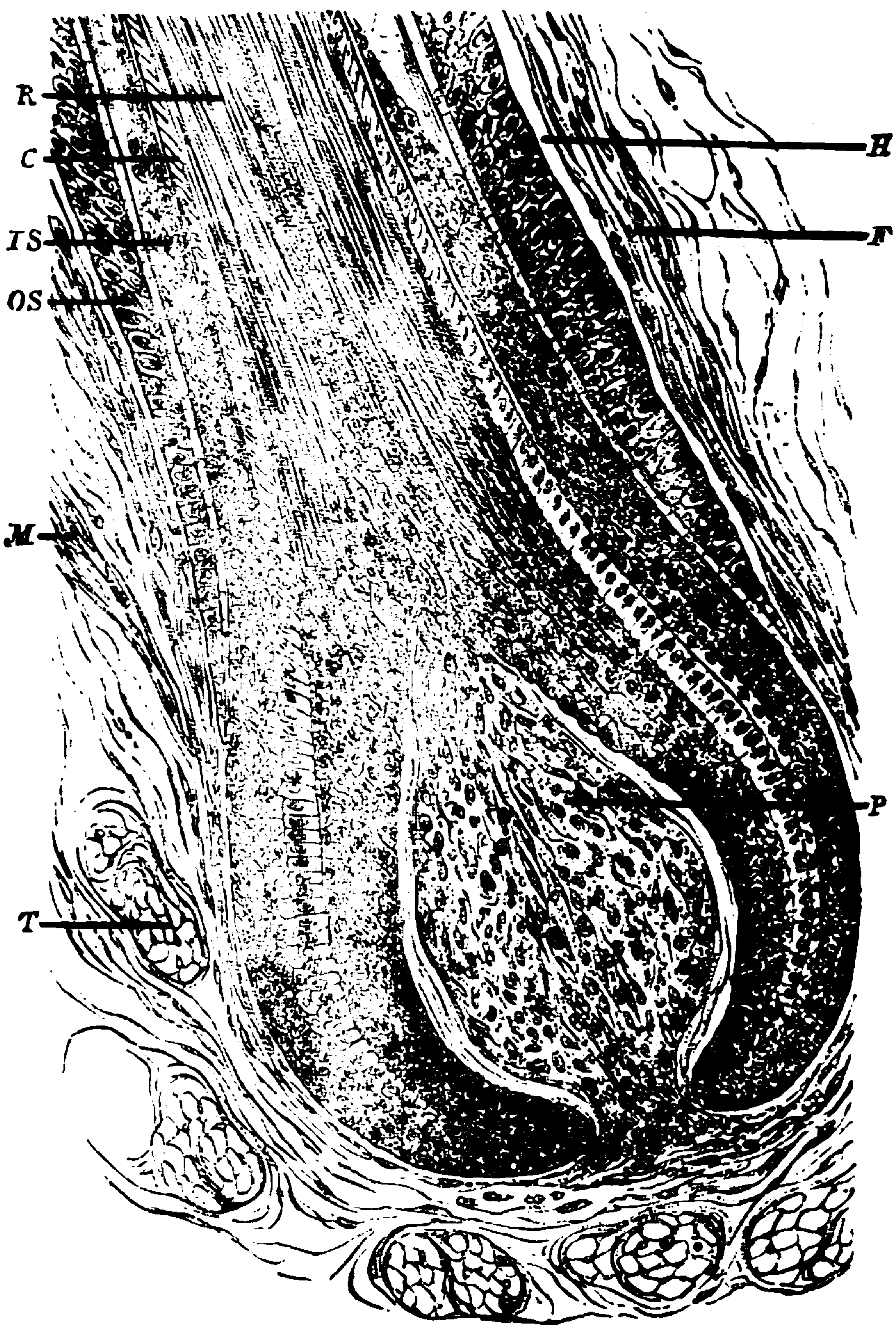


FIG. 236.—THE LOWER PORTION OF THE HAIR-POUCH, FROM THE LIP OF A KITTEN.

F, follicle; *T*, transverse sections of connective-tissue bundles of derma; *M*, arrector pili muscle; *IS*, inner root-sheath; *OS*, outer root-sheath; *P*, papilla; *C*, cuticle; *R*, root of hair; *H*, hyaline, or so-called structureless, membrane. Magnified 300 diameters.

globular, indifferent, or medullary corpuscles, which hold a varying amount of pigment, and fill also the central portion of the root, the so-called medullary space, which even in strong hairs

may be absent. The upper portion of the outer root-sheath is composed of stratified epithelia, the most external layer being distinctly columnar. This columnar row is the last one left, as the outer root-sheath approaches the region of the bulb, and, gradually becoming thinner, is at length entirely lost at the height of the bulb, whose formation it does not enter at all. The boundary line between the outer and the inner root-sheath is marked by the presence of a so-called structureless or cuticular membrane. External to the outer root-sheath we find the follicle, a connective-tissue formation, with interspersed circular muscle-spindles, connected with those of the arrector pili muscle. Between the follicle and the outer root-sheath there is usually a broad homogeneous layer, which can be traced around the bulb of the root and the papilla of the hair.

The papilla of the hair is composed of a delicate fibrous or myxomatous connective tissue, freely supplied with plastids having the appearance of spindle-shaped nuclei, and traversed by a number of capillary blood-vessels. The apex of the papilla in our specimen is not distinctly separated from the epithelia of the hair. The line of demarcation, however, as a rule, is distinguished by the presence of a row of columnar epithelia or by the medullary corpuscles.

Outside of the follicle we find the fibrous connective tissue of the derma, built up by longitudinal and transverse bundles. At the bottom of the hair follicle, in the human skin, a longitudinal tract of fibrous connective tissue is often found, which runs in the direction of the hair, and carries the blood-vessels (G. Wertheim).

In comparing what I have said about the theory of the formation of the hair with specimens of the skin, a satisfactory congruence will be found. This theory, as I have taught for nearly seven years in my laboratory, will explain the fact that upon pulling a hair the inner root-sheath is drawn out simultaneously with the root. It furthermore explains the process of shedding and the new formation of the hair.

(8) *The Hair.* As before mentioned, the part of the hair implanted in the skin is called the *root*, while the portion projecting above the surface of the skin bears the name of *shaft*. Its main mass is composed of delicate, flat, nucleated, fusiform epidermal scales, which are firmly attached to each other, but may be isolated by soaking in dilute acetic acid. The darker the complexion of the individual, the greater is the amount of granular

pigment found both within and between the scales, which, in addition, hold a diffuse coloring matter, especially in red hair. Gray and blonde hair are without pigment granules. After being pulled out the hair shows minute air-bubbles in its substance; but there is no foundation whatever for the belief that the gray color of the hair is due to the presence of such air-bubbles. The original hue of the hair is caused by the pigment stored up in its medullary and horny portion, and corresponds to the amount of coloring matter present in the rete mucosum of the skin, as seen in leukopathia, vitiligo, and in variegated or pied animals. Unquestionably, the amount of pigment is closely connected with

O

S

FIG. 237.—POUCH OF THE HAIR FROM THE SCALP OF MAN, TRANSVERSE SECTION.

R, root of the hair; *C*, cuticle; *IS*, inner root-sheath; *Ss*, cuticular layer between the two root-sheaths; *OS*, outer root-sheath, S^1, hyaline basement-layer between outer root-sheath and follicle, *F*, follicle. Magnified 500 diameters.

the general nutrition of the skin and under the control of the so-called trophic nerves, as proved by the rapid turning gray of the hair in exhaustive diseases and after mental emotions. The shape of the hair is best studied in transverse sections. Flat hair exhibits, as a rule, a circular or oblong section, while in curled hair this is elliptical or uniform. (See Fig. 237.)

Shedding of the Hair. We know through A. Kölliker and

C. Langer that the young hair is formed around the old papilla. We know, besides, that at a certain height above the papilla there is a knob-like thickening (Henle), which corresponds to the bulb of the falling hair. The fact added by me is that the new growth of a hair takes place exclusively within the inner root-sheath. The inner root-sheath, below the bulb of the old hair, which is fringed by the torn epidermal scales, becomes gradually widened. At the bottom of the pouch it turns upon itself and produces the bulb, which is composed of medullary, or indifferent or embryonal, corpuscles. The boundary between the two portions of the inner root-sheath is established by the cuticle, which, below the bulb of the old hair, is composed of

FIG. 238.—DIAGRAM OF THE PROCESS OF SHEDDING OF THE HAIR.

F, follicle, *M*, arrector pili muscle; *P*, papilla of hair; *B*, bulb of hair, *IS*, inner root-sheath, *OS*, outer root-sheath; *C*, cuticle; *R*, root; *OH*, old hair still in connection with *(YH)* the young hair rowing from the bulb.

columnar epithelia. The pigment, where there is any, lies exclusively in the central portion of the inner root-sheath, from which arises the future hair. The outer root-sheath takes no part in the new formation of the hair. The smooth muscles of the follicle are evidently concerned in the process, inas-

much as through their contraction a narrow neck is established around the young hair, as first suggested by Biesiadecki. (See Fig. 238.)

The Development of the Hair can be first traced at the end of the third month of intrauterine life. The epithelial investment of the skin produces a knob-like prolongation downward, while later an extension of the connective tissue is formed, which lifts the bottom of the epithelial knob, and produces the papilla. The epithelia are originally all medullary in character, and from the medullary corpuscles, by elongation and mutual flattening,

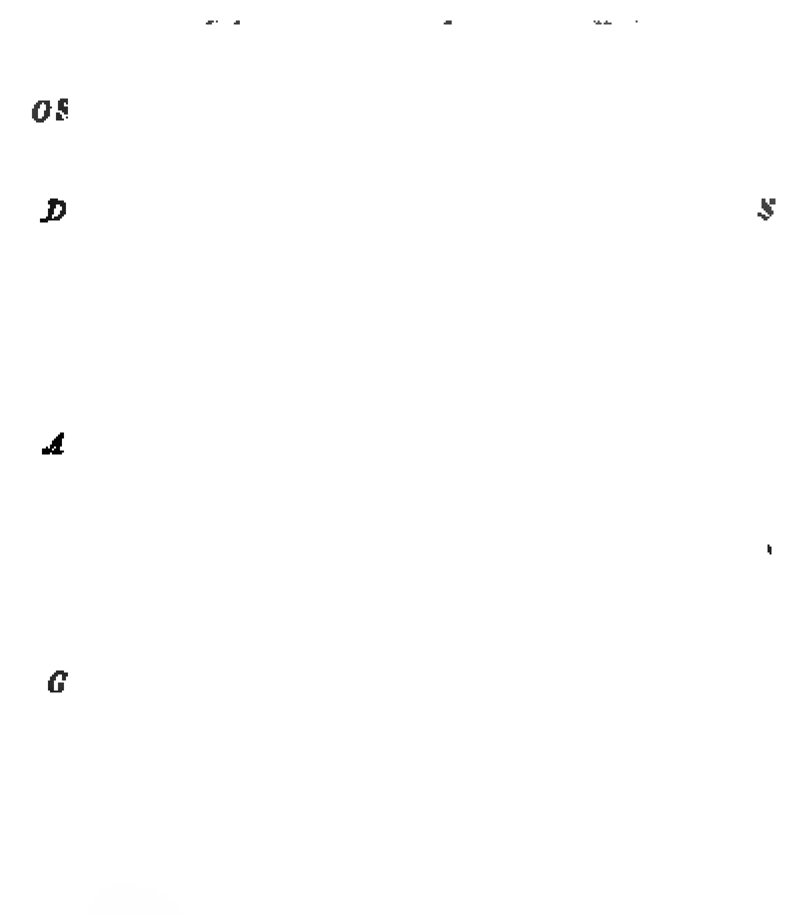


FIG. 239.—SCALP OF MAN. VERTICAL SECTION.

R, root of hair; *IS*, inner root-sheath; *OS*, outer root-sheath; *G*, sebaceous gland; *D*, duct of the sebaceous gland; *A*, acarus folliculorum within the duct of the sebaceous gland. Magnified 200 diameters.

arise the elements composing the hair in the center of the knob, and also the root-sheaths at its peripheral portion.

(9) *The Sebaceous Glands.* The acinous sebaceous glands are formed from the outer root-sheath of the hair, and are usually in close relation to the hair. Sebaceous glands without hair are found in the areole around the nipple of the female breast, in the glans and the prepuce of the penis, in the nymphæ and

the prepuce of the clitoris. In the palms of the hands and the soles of the feet there are no sebaceous glands.

The relation of the glands to the hair varies greatly according to the size of the latter. The largest sebaceous glands are found in the naso-labial folds; here the fine lanugo hairs are subordinate formations, piercing the duct at an acute angle. At the extensor surfaces of the extremities and the posterior aspect of the trunc the sebaceous glands are elongated; in the axillæ they are flattened. On the scalp they are sometimes small, pear-shaped structures, and usually two of them empty into one hair-pouch, both being under the control of the same fan-like arrector pili muscle (Hesse). (See Fig. 239.) Sometimes, however, they attain a considerable size. In horizontal sections of the

FIG. 240.—SCALP OF MAN. HORIZONTAL SECTION.

H, root of hair, surrounded by its sheaths; *S*, sebaceous gland; *F*, follicle common to the hair-roots and the sebaceous glands. Magnified 200 diameters.

scalp we find groups composed of roots of hair and sebaceous glands, inclosed by the fibrous connective tissue of the derma, which sends delicate prolongations between the epithelial formations. The numerous acini visible in this situation do not correspond to single sebaceous glands, but to their branching lower ends. (See Fig. 240.)

In specimens of sebaceous glands, preserved in a chromic acid solution, the acini appear filled with fat, and the lining

epithelia are not easily discernible. Treatment with alcohol and turpentine brings the nucleated cuboidal epithelia distinctly to view, and in such specimens we also recognize that the acinus contains several layers of epithelia. In many sebaceous glands a parasitic mite is found, the acarus or demodex folliculorum, which is harmless, however.

(10) *The sudoriparous glands* are composed of a single coiled tubule, lying in the deep parts of the skin, usually near or in the subcutaneous tissue; the same tubule produces not only the coil, but the duct also, the difference being that the coiled portion of the tubule is lined with cuboidal epithelia, and the duct, up to the point where it reaches the rete mucosum, with the columnar variety. If we assume a prolongation of the outer epithelial layers into the depths of the derma, the formation of the sweat-gland is easily understood.

The sudoriparous glands are present all over the skin, varying in size in different individuals and in different localities; they are most numerous in the palms of the hands and the soles of the feet; the largest are found in the axillæ and in the neighborhood of the anus; they are not found in the glans penis and the inner surface of the prepuce. They are all inserted in an oblique direction in the derma, corresponding to the general arrangement of the connective-tissue bundles. Their orifices on the surface of the skin, in the furrows between the papillary ledges, are perceptible to the naked eye. The sweat-glands at the borders of the eyelids—the so-called glands of Moll—have, it is maintained, spiral terminations, instead of coils, and empty into the hair-pouch of the cilia. The ceruminal glands of the external auditory canal are constructed like sudoriparous glands, but secrete an unctious substance, which is commonly called ear-wax.

By cutting through the coil, transverse, oblique, and longitudinal sections of the tubule are produced. The lining epithelium is, in this situation, a cuboidal or short columnar epithelium in one layer, attached to a delicate hyaline membrane. In the empty condition of the gland the caliber is very narrow, and the cement-ledge of the epithelia is plainly marked at the surface bounding the caliber. (See Fig. 241.)

The connective tissue carries a large number of capillaries, and produces a capsule surrounding the coil, and prolongations passing around the tubule through its whole extent. In the connective tissue there are seen smooth muscle-fibers, which are very

numerous around the sudoriparous glands of the axillæ, where they form an almost continuous layer, which expands into a flat, sheet-like arrangement.

The diameter of the duct, at its beginning, does not exceed that of the tubule within the coil; very soon, however, it becomes decidedly broader, and shows a single stratum of columnar epithelia (not stratified, as some authors claim) and a wide caliber. These conditions are particularly marked in cross sections of the duct, such as are often seen in the derma. Delicate bundles of connective tissue, arranged longitudinally, accompany the duct; no smooth muscle-fibers are present in them. The duct leads in a slightly devious course to a depression between two papillæ, and in this situation is composed of stratified epithelia, a forma-

FIG. 241.—COIL OF THE SWEAT-GLAND.

S, tubule lined by cuboidal epithelia; *T*, central caliber of the tubule; *D*, beginning of the duct; *C*, connective tissue with injected blood-vessels. Magnified 500 diameters.

tion of the rete mucosum, prolonged to a varying depth of the duct. After having reached the epidermal layer, the duct is lined by a single layer of flat epithelia, its caliber being considerably widened, especially at its orifice at the surface of the skin. Within the epidermal stratum the duct shows windings which are scarcely perceptible in places where the epidermis is thin, while in situations where the epidermis is very thick, such as the palms of the hands and the soles of the feet, these spiral

windings have the characteristic corkscrew-like appearance. (See Fig. 242.)

(11) *The nails* are flattened, plate-like formations of a horny or epidermal character. The skin is elevated along the lateral borders of the nail, and produces at the posterior end of the nail a broad pouch, termed the matrix, which incloses the root of the nail. According to Unna, the matrix proper of the nail is only the posterior portion of the derma, commencing with the anterior curved line of the lunula; and only the bottom of the furrow serves as a matrix to the anterior portion of the nail. H. Hebra does not consider the lunula as a part of the matrix, for it is destitute of papillæ, and scantily supplied with blood-vessels

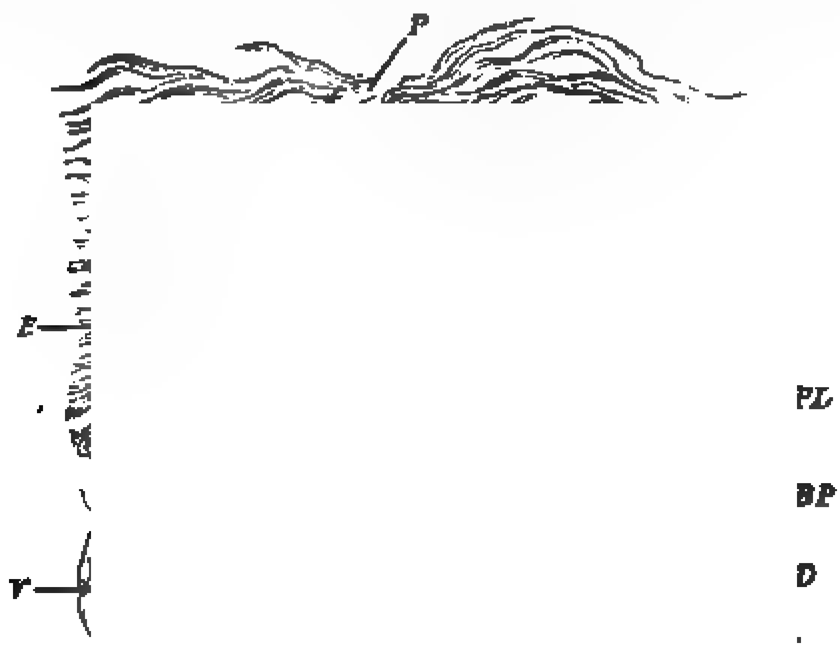


FIG. 242.—DUCT OF THE SWEAT-GLAND WITHIN THE EPITHELIAL LAYERS OF THE SKIN.

BP, papilla with injected blood-vessels; *V*, valley between two papillæ, *D*, duct in the rete mucosum; *EE*, epidermal layer, *PL*, coarsely granulated epithelia, deeply stained with carmine; *P*, duct with corkscrew windings in the epidermal layer. Magnified 200 diameters.

The papillary layer of the skin subjacent to the nail is highly developed, the papillæ being arranged in parallel rows corresponding to the long axes of the fingers and the toes. The papillæ are shallow in the region of the matrix, but increase in size toward the free portion of the nail, especially toward its lateral borders. At the inner surface of the lateral ledges, and in the depth of the lateral furrow, they are replaced by the papillæ of the skin. The derma forming the papillæ is composed of coarse, dense bundles, inclosing a comparatively small number

of fat-globules, and blending with the periosteum of the last phalanx. In this situation the vascular supply is strikingly large. (See Fig. 243.)

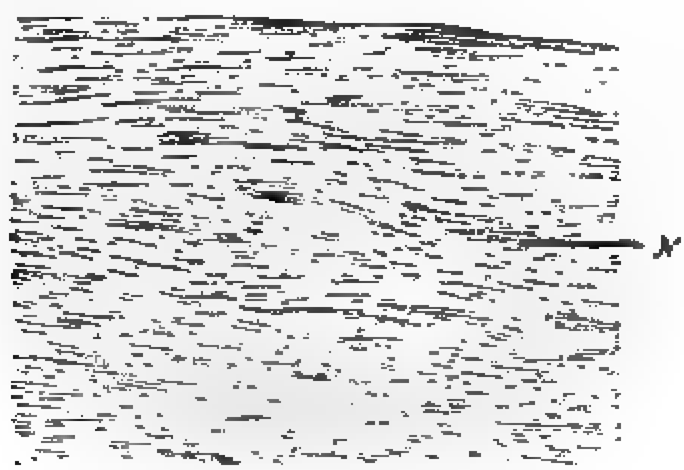


FIG. 243.—NAIL OF FINGER, VERTICAL SECTION, RECTANGULAR TO THE LONG AXIS OF THE FINGER.

P, papillæ with blood-vessels. *B*, rete mucosum. *N*, horny epidermal scales. Magnified 100 diameters.

The derma is covered by an epithelial layer, identical with that of the rete mucosum, and filling the valleys between the papillæ in such a manner that the upper boundary of the rete mucosum exhibits only a fluted contour. According to C. Toldt, the so-called lunula of the nail, most distinctly marked on the nail of the thumb, is caused by a lessened transparency of the nail, due to the rete mucosum producing, in this situation, a broad layer of a uniform distribution. The rows of the papillæ are much less developed in the region of the lunula than in the rest of the matrix. By scraping with the knife the lower surface of the detached nail, the lunula disappears, and the nail becomes uniformly transparent.

The nail substance consists of horny epithelia, of which the lower ones exhibit indistinct nuclei, while the outermost resemble epidermal scales. In the region of the root a gradual tran-

sition from the epithelia of the rete mucosum into the horny epithelia takes place.

In the lateral portions of the nail, where papillæ are absent, the rete mucosum of the skin, forming the ledge and the furrow, passes into that of the nail through irregular, branching prolongations, which exhibit marked layers of epithelia, more or less endowed with life. In this situation the papillæ of the nail are lost, but are replaced by very small and elongated papillæ, which belong to the skin and stand in an oblique direction to the rows of the papillæ of the nail. A true transverse section through the nail will exhibit within the furrow oblique and transverse sections of the slender papillæ of the skin. (See Fig. 244.)

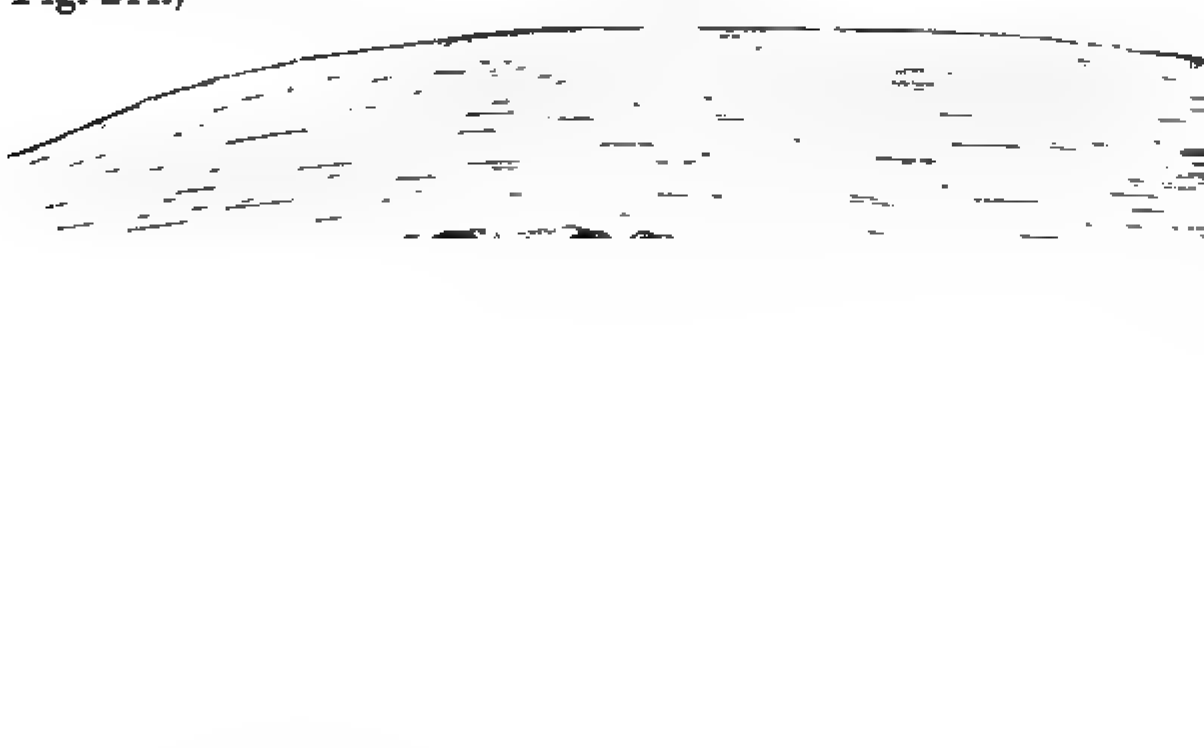


FIG. 244.—IMPLANTATION OF THE NAIL AT ITS BORDER.

P, papillæ, decreasing in size toward the middle line; *R*, rete mucosum, which broadens toward the border of the nail, and forms irregular prolongations, *R*¹; *E*, epidermal layer of middling consistence; *N*, plate of the nail. Magnified 50 diameters.

The epidermis of the skin produces a pointed prolongation, which overlaps the borders of the nail; this prolongation is most clearly marked along the posterior border.

(12) *The lacteal glands* are accessory formations of the skin. According to C. Langer, who has made careful researches on the development, the structure, and involution of the lacteal glands, they begin to form in the third month of embryonal life, and in the fifth month present radiating tubules, with club-like terminations. The tubules open into a shallow depression of the skin, the

nipple being absent. In the new-born infant the tubules branch several times, and all of them show clavate termination. The ramifications increase in number, in both sexes, up to the twelfth year, without the production of acini, the main mass consisting of connective tissue, destitute of fat-globules.

At the time of puberty in girls the mammary gland develops into a discoid body, composed of dense, fibrous connective tissue, without fat; the radiating ramules exhibit in this period acinous terminations at the periphery of the organ, and only here is the lobular structure marked.

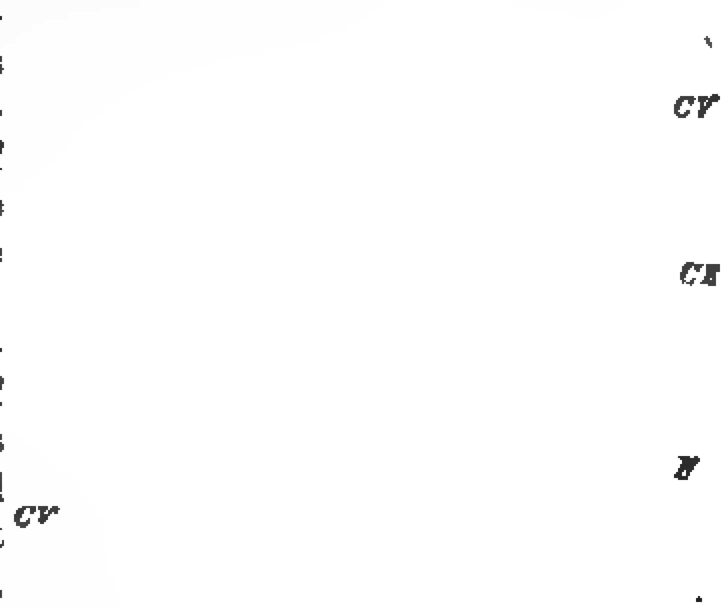


FIG. 245.—ACINI OF THE FEMALE BREAST AT THE BEGINNING OF LACTATION.

CE, cuboidal epithelia, *F*, fat-globules, both within the epithelia and the caliber, stained black by osmic acid: *CV*, connective-tissue frame, with blood-vessels. Magnified 600 diameters.

In pregnancy a considerable development of the acinous glands takes place, especially toward the end, when about twenty ducts are found, emptying at the point of the nipple, and a corresponding number of lobules is produced by the free ramification of the ducts and the formation of numerous acini within one lobule. The ducts, before emptying, are widened into pear-shaped sinuses; their lining throughout the ramification consists of a single layer of columnar epithelium. The acini are lined with cuboidal epithelia, and at the beginning of lactation exhibit numerous fat-granules, both within the epithelia and the caliber. (See Fig. 245.)

In full lactation the lobules and the acini therein assume the largest size; the epithelia are scarcely perceptible, for most of them are transformed into fat, and upon being treated with turpentine usually show the frame of cement-substance, the nuclei, and numerous vacuoles (see page 332). After the period of lactation has passed, the acinous structure of the gland remains, the small acini surround the ducts in regular groups, and the connective tissue now contains a large number of fat-globules. In the matron a few ducts only are found, lined with

columnar epithelia, partly filled with minute fat-granules; acini are wanting.

In male adults the mammary gland exhibits a structure similar to that of the new-born infant; real acini do not exist, even though the gland may attain a considerable size.

The lowest layers of the rete mucosum of the nipple and its areole contain pigment granules; the papillæ are very large and branching, and have either capillary loops or tactile corpuscles. The derma is freely supplied with bundles of smooth muscle-fibers in a reticular arrangement; they are twined around the lacteal ducts in a vertical direction.

Within the areole the connective tissue of the derma and the subcutaneous layer is free from fat. During the latter months of pregnancy small granular elevations are found in the areole, which are sebaceous glands, emptying at the height of the granule. They have been erroneously described as accessory cutaneous lacteal glands. Occasionally they give rise to an active glandular new formation, with the production of a sebaceous adenoma.

*Inflammation of the Skin.** I have studied the process of inflammation of the skin in specimens from a syphilitic papule; from small-pox; from an ulcerating sac of umbilical rupture in a cat. I have investigated the terminations of inflammation in specimens of elephantiasis of the scrotum and of the labia majora. Inflammation as an accompanying process I have studied in the skin of the female breast in mastitis and cancer, and also in the skin covering different benign and malignant tumors, or directly involved in the formation of such tumors. The results in all these cases being almost identical in regard to the essential changes in the tissues of the skin, I can confine myself to the description of the inflammatory process in small-pox, of which I obtained six different specimens from the Blackwell's Island Hospital; among these were two of hæmorrhagic small-pox.

The coarser microscopical features in the formation of small-pox have been accurately studied by Auspitz and Basch. The essential structural changes observable with high magnifying powers of the microscope,—800–1200 diameters,—and which can be understood only upon the knowledge of the normal anatomy of the affected tissues, are as follows:

First, the epithelial layer, termed rete mucosum, appears slightly thickened in circumscribed spots; the swelling is due to a coarse granulation of the epithelia themselves. This granulation is produced by an increase of living matter within the epithelia, evidently through an augmented afflux of nourishing material during the stage of hyperæmia. The points of intersection of the net-work of living matter, the so-called granules, become enlarged, many of the nuclei are solid and shining, and at the same time the threads

* "Microscopical Studies on Inflammation of the Skin." A paper read before the American Dermatological Association at their meeting in New-York, August 27, 1879. Published in abstract in *The Chicago Medical Journal and Examiner*, October, 1879.

traversing the cement-substance, the formerly so-called "thorns," become thickened. The underlying papillæ are slightly enlarged in all diameters, partly owing to a dilatation and engorgement of their capillary blood-vessels, partly through a peculiar change of the bundles of the connective tissue and the bioplasson bodies between them. The latter look slightly enlarged, and in many instances coarsely granular; the former are partly transformed into bioplasson. In other words, where before bundles built up by a glue-yielding basis-substance were present, the reticulum of the living matter, before hidden in the relatively solid basis-substance, becomes visible again through a liquefaction or dissolution of this substance. No other proof of the presence of an exudation in this stage can be obtained, except the liquefaction of the basis-substance. *This stage of inflammation is termed "papular."*

Next, in the middle of the papule, on one or on several spots, the exudation makes its appearance; the outer or epidermal layer at no time participates in the morbid process. In some epithelia we notice an enlargement of the meshes of the living reticulum; the latter is first stretched, afterward torn apart, the granules being suspended in the liquid exudation. Where epithelia were present before, a small, irregular cavity is visible. If several such cavities have formed in a papule through a continuously increased accumulation of the exudation and destruction of the epithelia, the separating layers of the epithelia become compressed and produce septa, traversing the cavities. Such septa vary greatly both in number and width. The neighboring epithelia have a coarsely granular appearance. Many of them have lost the inclosing cement-substance, and are thus transformed into clusters, in which, through a considerable increase of the living matter, new shining lumps of different size appear, which are still in continuity with the neighboring reticulum by means of delicate threads — the so-called endogenous formation of new elements. The result of this process is the formation of an irregular cavity in the middle of the greatly widened rete mucosum, traversed by septa of compressed epithelia, and filled with an exudation, in which there are suspended numerous delicate granules, generally termed coagulated albumen, and a varying amount of irregular threads in the form of a felt-work, the coagulated fibrine. A few scanty plastids are also suspended in the exudation, perhaps remnants of the destroyed epithelia, perhaps immigrated inflammatory or colorless blood-corpuscles.

In this condition of the rete mucosum, the underlying connective tissue exhibits considerable changes. The papillæ have disappeared, evidently through the pressure from above. The transformation of the connective tissue into bioplasson has advanced, in some instances, to such a degree that the uppermost layers of the derma are replaced by numerous indifferent, or medullary, or inflammatory corpuscles, as a rule, clustered together. All these elements, however, are in an uninterrupted connection with each other through delicate filaments of living matter, fully analogous to those of the epithelia, and thus the inflamed tissue, though reduced into its medullary condition, still represents a tissue. The stage of the disease in which the changes just described had taken place is known as *the vesicular stage of small-pox.*

Lastly, pus-corpuscles appear in the cavity within the rete mucosum. The main mass of these doubtless arise from the epithelia traversing and bounding the cavity. Through the increase of living matter in the large number of epithelia, shining lumps appear, first homogeneous-looking, afterward through the intermediate stage of vacuolation transformed into nucleated plas-

tids, with a fully developed reticulum of living matter — the pus-corpuscles. The principal sources of pus-corpuscles, therefore, are the epithelia themselves, the endogenous formation. (See page 419, fig. 176.) How many of the pus-corpuscles appear through an immigration from below, from the inflamed connective tissue or from the blood-vessels, nobody can tell. The immigration is a sensible hypothesis only, without direct proof or foundation, while the endogenous formation can be directly traced in all its stages. The pus-corpuscles are coarsely granular, viz.: are supplied with a large amount of living matter at the points of intersection of the living reticulum in persons of a good, strong constitution; on the contrary, they are finely granular — that is, scantily provided with living matter — in persons of a weak, so-called scrofulous or tuberculous, constitution, or in persons debilitated by any acute or chronic disease. In the former instance the pus is thick and yellow, in the latter instance watery, serous, and pale. The subjacent connective tissue, as a rule, does not advance beyond its reduction into a medullary tissue. In some cases, however, the newly appeared and newly formed medullary corpuscles, which produce the infiltration of the derma to a varying depth, are also torn asunder, and thus represent pus-corpuscles, which, commingling with the pus which has sprung from the epithelia, take part in the formation of the abscess.

This stage of inflammation is known by the term *pustular stage of small-pox*, and represents the typical termination of the whole process. The pustule either bursts or its contents dry and produce the crust. So long as the inflamed derma remains in the condition of medullary tissue, so long as the medullary or inflammatory elements remain connected with each other, the new formation of a glue-yielding basis-substance in the shape of bundles of fibrous connective tissue will be accomplished, without the formation of a scar. If, on the contrary, a part of the connective tissue has been transformed into pus, and thus completely destroyed, the result will be a cicatrix. Mere epithelial suppuration heals without the formation of a scar, while suppuration of the connective tissue always produces a mark. The pigmentation of the skin, so common after small-pox, is due to the imbibition of the coloring matter of the red blood-corpuscles; or by changes of the directly extravasated red blood-corpuscles, both in the rete mucosum and the derma. Such extravasations occur in all severe cases of small-pox — in the highest degree, of course, in hæmorrhagic small-pox.

My observations on inflamed portions of skin have led me to the following conclusions:

(1) In epithelium, the first step of the inflammatory process consists in an increase of the living matter, both in the plastids and between them; the former produces the coarse granulation of the epithelia, the latter the thickening of the so-called "thorns" in the cement-substance. Any particle of living matter, both in the epithelia and between them, through a continuous growth, may lead to a new formation of the epithelial elements, with termination in hyperplasia of epithelium (psoriasis, squamous eczema, horny formations, etc.).

(2) In connective tissue, the first manifestation of the inflammatory process is the dissolution of the basis-substance and re-appearance of the bioplasson condition; by this process and the new formation of medullary elements, which may start from any particle of living matter, the inflammatory infiltration is established. The sum total of the inflammatory corpuscles,

which remain united with each other by means of delicate offshoots, represents an embryonal or medullary tissue. If the new formation of medullary corpuscles be scanty, resolution is accomplished by new formation of the basis-substance (erythema, erysipelas, etc.). If, on the contrary, the new formation of medullary elements be profuse, a new formation of connective tissue will result (hyperplasia, scleroderma, elephantiasis, etc.).

(3) Plastic (formative) inflammation may be accompanied by the accumulation of a larger amount of a serous or albuminous exudation in the epithelial layer (miliaria, sudamina, herpes), or in the connective tissue of the derma (urticaria). In both instances complete resolution will ensue.

(4) Suppuration in the epithelial layer of the rete mucosum is produced by an accumulation of an albuminous or fibrinous exudation, by which a number of epithelia are destroyed, and by new formation of pus-corpuscles from the living matter of the epithelia themselves. Epithelial suppuration heals without the formation of a cicatrix (eczema madidans et pustulosum, impetigo, pemphigus, variola).

(5) Suppuration in the connective tissue of the derma results from the breaking apart of the newly formed medullary corpuscles, which, being suspended in an albuminous or fibrinous exudation, now represent pus-corpuscles. Pus is a product of the inflamed connective tissue itself, and is always a result of a destruction of this tissue. Suppuration of the derma invariably heals through cicatrization (abscess, furuncle, acne, ecthyma, variola).

*Tumors of the Skin.** (1) *Myxomatous or mucoid tumors* are composed of a delicate fibrous reticulum, the meshes of which contain a jelly-like basis-substance and plastids varying greatly in size. They are frequently found on the skin as soft, jelly-like, sessile, or pediculated protrusions. They are often supplied with a large quantity of blood-vessels, and are then soft tumors, of a dark red color, the "myxo-angioma." Myxomatous tumors, having the structure of the thyroid body and called "lymph-adenoma" or "lymphoma," are very rare. They may occur in the subcutaneous tissue of the neck, but have no connection with the thyroid body itself.

(2) *Fibrous tumors* in all their varieties (see page 483), and also the combination of fibrous with myxomatous connective tissue, so called "myxo-fibroma," being, as a rule, scantily supplied with blood-vessels, are common tumors of the skin, appearing as hard, sessile nodules and nodes *(hard fibroma)*, or as pedunculated tumors, sometimes scattered over the entire tegumentary surface *(fibroma molluscum)*; as tumors of varying size, and softer consistence *(soft or myxo-fibroma)*; as pigmented flat elevations of the skin *(nævi)*; or as scar-like, irregularly branching, sometimes freely vascularized new formation *(keloid)*. The peculiarity of these entirely benign tumors is that after extirpation they sometimes recur, and even the scar, after the removal of a fibroma, may assume the features of a keloid.

(3) *Chondroma* and (4) *Osteoma*, do not occur on the skin.

(5) *Myeloma* (sarcoma), in its two principal varieties — viz.: globo-myeloma and spindle-myeloma — is of somewhat infrequent occurrence; in the derma it usually appears as *fibro-myeloma*; rarely as a pigmented *melanotic myeloma*. Such tumors originate as nodules of the skin, sometimes accompanied with inflammatory symptoms, and their malignancy is proved by their

* A paper read before the American Dermatological Association, at their meeting in Newport, R. I., August 31, 1880. Printed in abstract in "Archives of Dermatology," Philadelphia, October, 1880.

rapid growth, by a new formation of nodules in the vicinity of the primary tumor, and by their recurrence after extirpation. An original myxo-fibroma, after repeated extirpation, may gradually assume the features of fibro-myeloma. The vascular supply of myeloma is sometimes scanty, at other times abundant. Some of these tumors multiply rapidly all over the skin, especially in the subcutaneous tissue, and some may, after reaching a certain size, disappear, while new nodules may form in other localities. The melanotic variety usually starts in the skin of the hands and the feet, and in a comparatively short time invades large portions of the surface of the body, and never admits of a cure. After extirpation, many of these tumors recur with great obstinacy, in the scar or in its vicinity, and prove more malignant with each re-appearance, until at last an operation becomes impossible. The patient dies, with symptoms of inanition, from the exhausting waste of living matter within the rapidly growing tumor, or from secondary formations in internal organs.

(6) *Lipoma* is a common type of tumor, occurring in the subcutaneous tissue, evincing some predilection for the posterior aspect of the body, and sometimes appearing as a diffuse accumulation of fat-tissue in the female breast. Lipoma combines with myxoma or myxo-fibroma, constituting the variety called "cutis pendula," or "leontiasis," which sometimes attains enormous size.

(7) *Angioma*, in its three varieties, is found in the skin. Simple and lobular angioma is usually seated in the derma, while the cavernous angioma, which is rarer, generally starts in the subcutaneous tissue. These tumors are all easily compressed, the blood disappearing, but returning when the pressure is removed. The dark red or bluish-red color is, as a rule, a marked feature, though wanting in the deeply situated cavernous tumors. New formations of lymph-vessels — the so-called *lymph-angioma* — occur in the tissue of the derma; the cavernous *lymph-angioma* is a rare formation in the subcutaneous tissue.

(8) *Myoma* has been observed by Virchow and others, usually occurring as small, flat, erectile tumors, in the skin around the nipple and in the scrotum. No case has as yet come under my observation.

(9) *Neuromata* appear in the skin as nodules, not attaining a large size, but characterized by their excessive painfulness. The great majority of these tumors are fibrous in structure, starting from the perineurium, and separating the medullated nerves.

(10) *Papilloma* is often found on the hands as simple *warts;* on the genitals as condylomata, and in other localities, though rarely, as hairy and *warty moles* (nævus verrucosus). The latter variety is congenital, while all other warty tumors are acquired, being due to some local irritation. I have seen the so-called venereal warts, on the skin of the back, evidently produced by transmission of the blennorrhagic secretion; on the chin — conveyed probably by the barber — and on the forehead and eyelids of a child — infected by the nurse. A peculiar feature of these tumors is that they are difficult to eradicate. Sometimes, in advanced age, they change their nature and become cancerous, especially in the face.

(11) *Adenoma* appears almost exclusively in the skin as adenoma of the sebaceous glands. Adenoma of the sudoriparous glands has been described by Verneuil only, and its existence is very doubtful. A variety of acinous adenoma, starting from the lacteal glands, is very common in the appendage

of the skin, the female breast. In tumors which are either sessile or pediculated—*molluscum sebaceum*—the racemose sebaceous glands are sometimes enormously augmented, while the interposed fibrous connective tissue is considerably diminished. The epithelium sometimes undergoes a colloid or waxy degeneration, producing large, shining, homogeneous, even stratified bodies, which were thought to be characteristic of *molluscum contagiosum*.

Cystic tumors are secondary formations of adenoma; they are filled with a serous liquid *(serous cyst)*, with a viscid, colloid, honey-like liquid *(melicéris)*, with a soft, fatty, offensive paste *(sebaceous cyst)*, or with a half-dry, viscid, slightly rancid mass *(dermoid cyst)*. It is very doubtful whether simple obstruction of a duct of a gland will ever give rise to the formation of a cyst, unless previous new formation of epithelium be present, the secondary changes of which give the characteristic properties to the contents of a cyst. *Sebaceous cysts*, so-called wens, are of frequent occurrence, most commonly in the skin of the scalp and of the face; they are sometimes present in a very large number. The sebaceous matter is inspissated and infiltrated with lime-salts in cysts termed *milium*.

(12) *Carcinoma*, in all its varieties,—flat, nodular, papillary, and plexiform epithelioma, scirrhus, and medullary cancer,—is observed in the skin. It is obvious that terms like "alveolar cancer," "epithelial cancer," "plexiform cancer," "epithelioma," etc., are misnomers, as every cancer is necessarily alveolar, and is an epithelioma. We have no reason to confine the name "epithelioma" to cancers of the skin, as in this tissue all varieties occur.

Flat cancer (so-called "rodent ulcer") is usually seen in the skin of the face, never producing exuberant growths; but by continuous ulceration it penetrates into the deeper parts and gradually destroys all the tissues. It is the least malignant form of carcinoma, and never produces secondary tumors. *Nodular cancer* (so-called "epithelioma") is of frequent occurrence in the skin, usually starting in localities which have been the seat of a long-continued though slight irritation. *Papillary cancer* (so-called cauliflower cancer) is rare, and appears whenever an exuberant growth of circumscribed portions of the tumor takes place toward the surface. *Scirrhus* and *medullary* carcinoma may grow on any part of the surface of the body, more particularly in the female breast. *Melanotic carcinoma* is rare. In very rapidly growing carcinoma epithelia do not develop, and the tumor remaining in the stage of the so-called medullary or inflammatory infiltration exhibits the features of globo-myeloma. This is especially marked in the rapidly growing so-called *lenticular cancer* (cancer à cuirasse) of the skin.

XV.

THE DIGESTIVE TRACT.

THE digestive tract is a continuous canal extending from the mouth to the anus, widening into the cavities of the mouth, the pharynx, and the stomach. Its walls are composed of connective tissue, and either striated or smooth muscle-fibers, and lined with epithelium, which is partly stratified and partly arranged in a single layer. The beginning and termination of the digestive tract are under the control of voluntary striped muscles. The flat muscle-layers keep the canal closed, unless solid, liquid, or gaseous material separates its walls and temporarily makes the caliber patent. All portions of the canal are in a high degree extensible.

The characteristic feature of the mucous membrane covering the whole length of the tract are stratified epithelium in the walls of the mouth, the pharynx, the œsophagus, and the lowest portion of the rectum; flat epithelium in the wall of the stomach, and a single columnar epithelium throughout the intestines. Delicate fibrous, and partly myxomatous, connective tissue, freely supplied with blood- and lymph-vessels, is found in the walls of the oral cavity, forming papillæ, which reach their highest development in the mucosa of the tongue; and are also present in that of the pharynx and œsophagus. Connective tissue also produces the filiform elevations in the small intestine and the projections and folds in the large intestine; besides all folds occluding the caliber of the canal when in an empty condition. The connective tissue surrounds the epithelial prolonga-

tions—*i. e.*, acinous mucous glands in the cavity of the mouth, the throat, the œsophagus, in the lowest portion of the rectum, and in the walls of the duodenum. It also holds the tubular pepsine-glands of the stomach and the tubular intestinal glands in the small and large intestine. The connective tissue forms, especially in youth, a layer of lymph-corpuscles, the so-called "adenoid layer" of myxomatous structure, which is permanent in the villosities of the small intestine, and accumulates here in the solitary follicles and the follicular patches. The mucosa, in many portions, has a circular and longitudinal layer of smooth muscles of its own; while the canal is everywhere surrounded

FIG. 246.—LIP OF A CHILD. VERTICAL SECTION.

E, epidermis; *R*, rete mucosum: *PP*, papillæ; *D*, derma, with injected blood-vessels. *M*, striped muscle-fibers. Magnified 200 diameters.

by a circular and longitudinal layer of striated or smooth muscle-fibers, with additional oblique layers in the œsophagus and stomach. The loose fibrous connective tissue, which unites the mucosa to the muscle, is termed the *submucous layer*, and contains, besides a varying amount of lymph-corpuscles, larger blood- and lymph-vessels and numerous nerves in plexiform arrangement, holding scattered or grouped ganglionic elements.

In the abdominal cavity, the outermost layer of the digestive tract is formed of connective tissue and lined with endothelia—the peritoneum.

The salivary glands, pancreas, and liver—glandular formations which aid in the digestive process—are situated along the tract, and empty their secretions into its cavities.

(1) *The Oral Cavity.* The lips are composed of a dense, interlacing fibrous connective tissue, of which the lower portions are connected with numerous striped muscles, and the upper portions produce the papillæ, sometimes showing bifurcating apices,

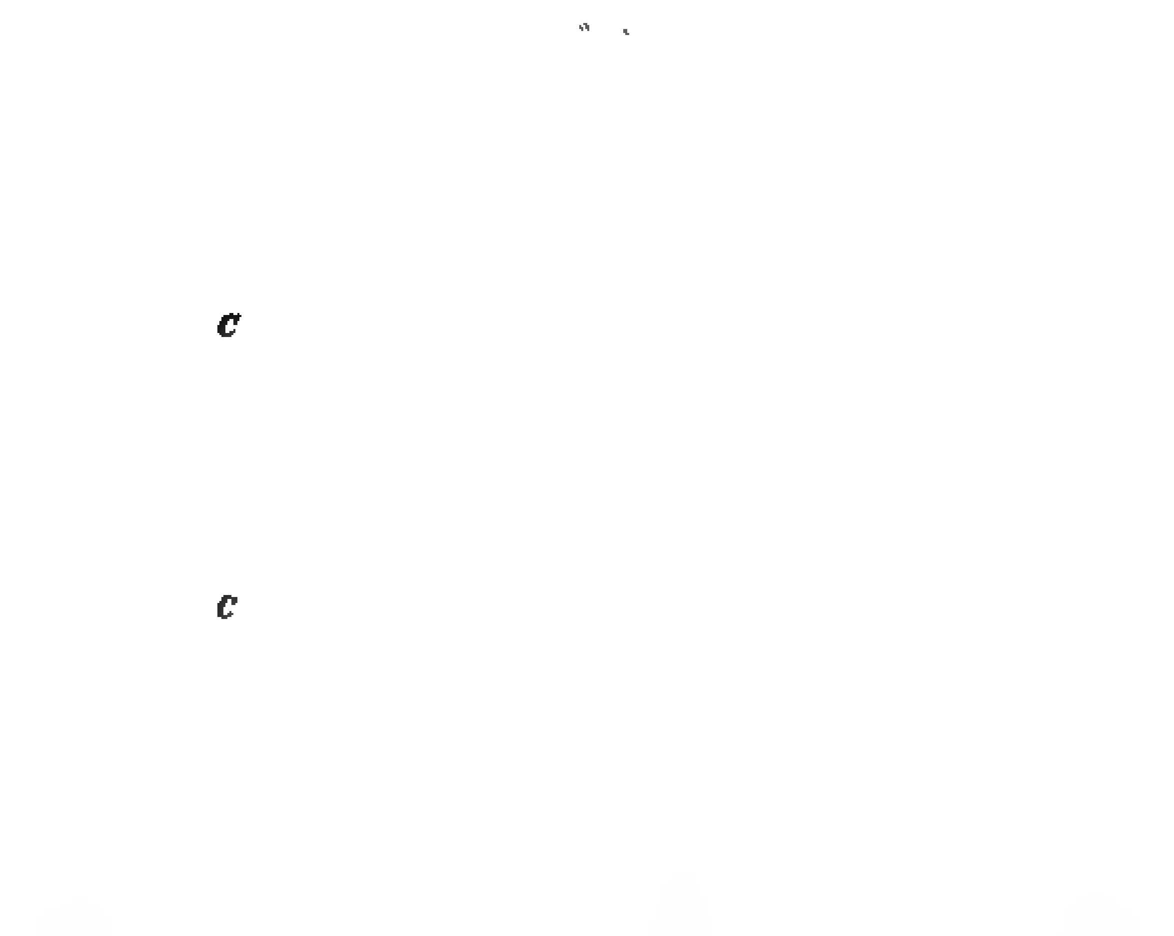


FIG. 247.—PAPILLA FROM THE LIP OF A CHILD.

CE, columnar epithelium, nearest to the connective tissue; *CF*, connective tissue, crowded with plastids; *A*, arteriole; *CV*, capillary loops, *V*, vein. Magnified 600 diameters.

and arranged in alternating large and small ones. (See Fig. 246.) The capillary reticulum of the large papillæ is very dense, and can be traced in direct connection with arterioles and veins. The vermilion color of the lips is due to the large number of capillaries. Within the papillæ the connective tissue is composed of delicate fibers, with comparatively numerous plastids, which usually have the size and appearance of nuclei. (See Fig. 247.)

The epithelium is continuous with that of the skin, and is stratified; the surface of the lips, however, appears smooth, because the epithelial cover does not follow the curves of the papillary elevations. The same peculiarity is found all over the oral mucosa. The epithelium sends prolongations into the connective tissue forming the racemose mucous glands, which, on the inner surfaces of the lips, are very large, and visible to the naked eye. Similar formations are found in the whole mucosa of the oral cavity.

The mucosa of the *oral cavity* is thickest on the hard palate, especially its posterior portion, and intimately connected with the subjacent periosteum. Very coarse bundles of fibrous connective tissue, blending with the periosteum, compose the gums, on which large papillæ are also found. In the floor of the oral cavity the connective tissue is comparatively loose, and the stratified epithelial layer thin; here and on the reduplications of the mucosa (frenulum linguæ, arcus glosso-palatinus, etc.) the papillæ are imperfectly developed. In the epithelial layer of the soft palate and palatine arches bud-like formations are found, similar to those of the circumvallate papillæ of the tongue. Many papillæ contain terminal nerve-buds (Krause's bulbs), connected with medullated nerve-fibers. Such structures are found in larger numbers on the inner surface of the lips, and on the anterior surface of the soft palate.

(2) *The tongue* is a bulky mass of striped muscles. Its covering mucosa is smooth on the lower surface, while the upper is abundantly provided with numerous large papillæ, and in this situation the stratified epithelial investment follows the papillary curves. Three varieties of papillæ are found on the tongue—viz.: filiform, fungiform, and circumvallate.

(a) The *filiform papillæ*, the most abundant, occur over the entire upper and anterior surface of the tongue; they are long and slender (1–2 mm. in length), and composed of connective tissue, dividing at the apex into a varying number of thread-like offshoots. They are largest in the middle of the upper surface of the tongue, especially toward the location of the circumvallate papillæ, while at the point and the lateral borders of the tongue they become smaller. In children they are comparatively much less developed than in adults. The stratified covering epithelium produces hair-like elongations, which are composed of flat, horny epithelial bodies corresponding to the projections of the connective tissue; such projections are wanting in children and on the

filiform papillæ of the lateral border. Terminal nerve-bulbs have been found at the bases of these papillæ. (See Figs. 248 and 249.)

(b) The *fungiform papillæ* are semi-globular or oblong formations scattered between the filiform papillæ (usually not exceeding one mm. in breadth and height), and arising from the level of the mucosa with a slightly narrowed neck. Toward their circumference the connective tissue produces a number of smaller so-called secondary papillæ, which are not marked on the outer surface of the thin epithelial investment. Sometimes the body of the papilla is cylindrical, without a neck, and the epithelium may assume features resembling those of the filiform papillæ, though

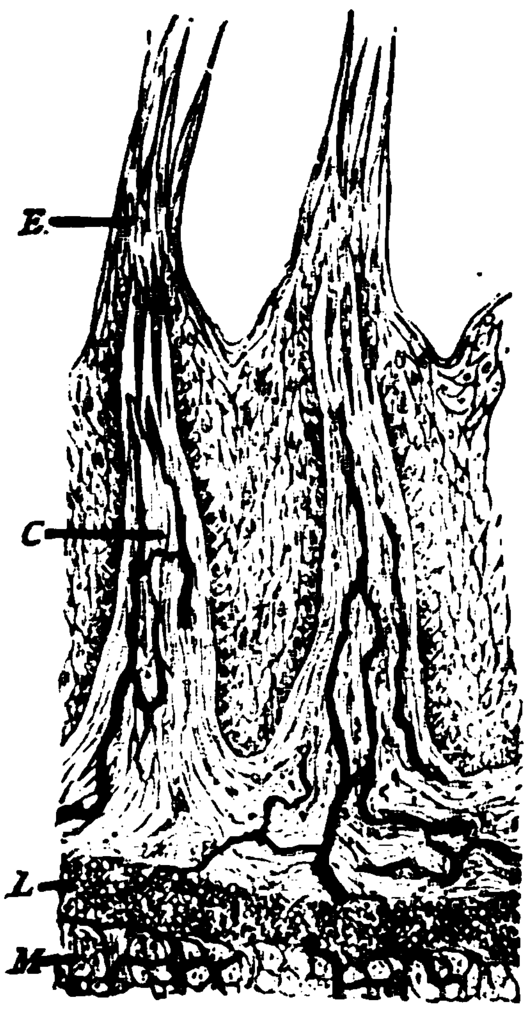


FIG. 248.—FILIFORM PAPILLÆ OF THE TONGUE OF MAN.

E, layer of horny epithelia; *C*, connective tissue with injected blood-vessels; *L*, lymphatic (adenoid) layer; *M*, striped muscles. Magnified 150 diameters.

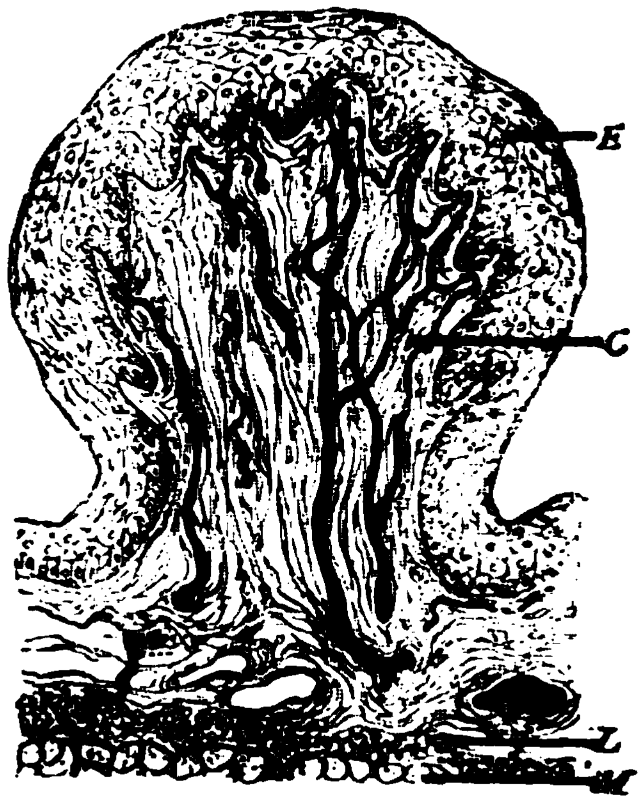


FIG. 249.—FUNGIFORM PAPILLA OF THE TONGUE OF MAN.

E, epithelial layer; *C*, connective tissue with injected blood-vessels; *L*, lymphatic (adenoid) layer; *M*, striped muscles. Magnified 150 diameters.

the prolongations are never numerous, and usually short and broad. Such papillæ are described as *conical*. Terminal nerve-bulbs are found at the bases of the secondary papillæ.

(c) The *circumvallate papillæ*, situated at the posterior part of the upper surface of the tongue, represent cylindrical elevations (1–2 mm. in height and 1–3 mm. in width), which are surrounded by a wall of the mucosa, and separated from this wall by a fur-

row. The furrow may divide the central papilla into two parts, or be very shallow. The secondary papillæ are present on the upper surface of the central papillæ only. The smooth epithelial investment in the lateral portions of the papilla, and also of its surrounding wall, contains peculiar bud-like formations (Schwalbe, Lovèn)—the *gustatory buds.* (See Fig. 250.) These are composed, at their periphery, of large, imbricated, so-called covering epithelia, while in the center of the bud delicate spindle-shaped, so-called gustatory, epithelia are inclosed. Their connection with non-medullated nerve-fibers has not as yet been conclusively proved. The apex of the gustatory bud is marked by a shallow depression. The ledges along the lateral borders of the tongue are called *papillæ foliatæ*, and are composed of a number of coal-

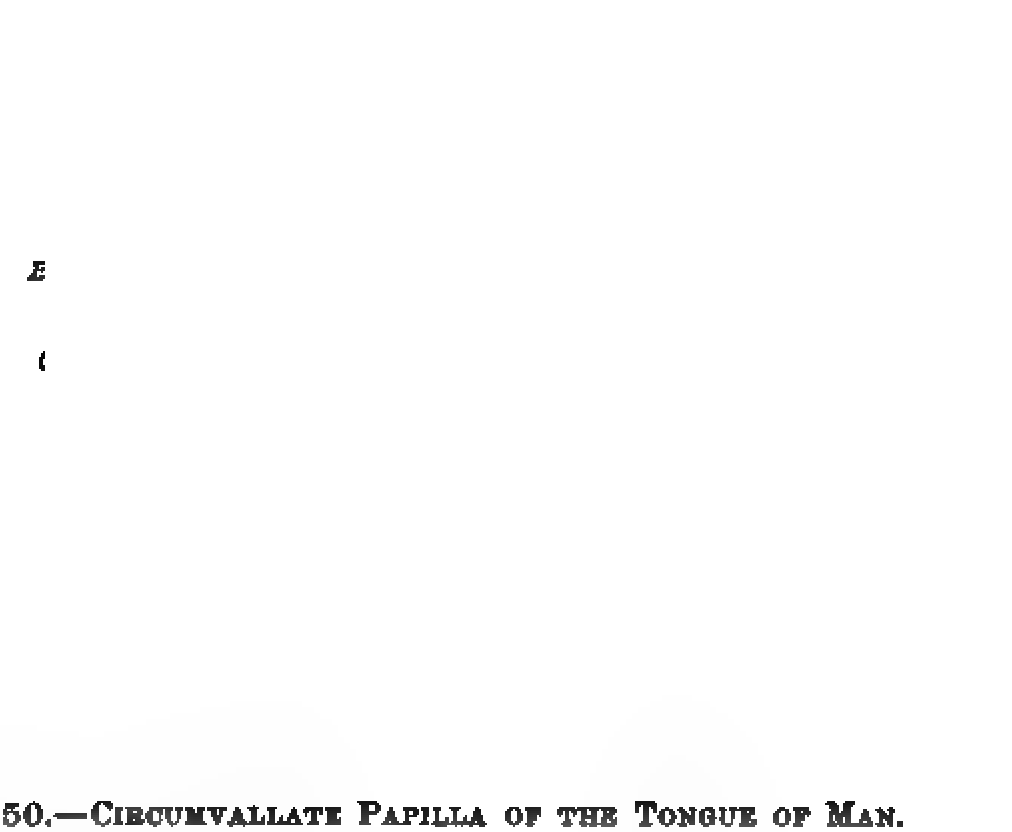


FIG. 250.—CIRCUMVALLATE PAPILLA OF THE TONGUE OF MAN.

E, epithelial layer; *G*, gustatory bud, *C*, connective tissue with injected blood-vessels, *M*, mucous gland with duct. Magnified 150 diameters.

esced papillary formations of the mucosa, with interspersed fungiform papillæ. In these ledges, which in man are not constant formations, gustatory buds have also been found.

The *glandular prolongations* of the epithelium, covering the tongue, are simple acinous and racemose *mucous glands*, similar to those of the mucosa of the oral cavity in general. They are large in the neighborhood of the circumvallate papillæ, and ramify between the superficial muscle-bundles; some of them empty in

the furrow of the circumvallate papillæ. On the anterior portion of the tongue mucous glands are found only along the lateral border, which coalesce into a larger group at the apex of the tongue.

At the posterior portion of the mucosa of the tongue, where papillæ are not present, a varying number of nodular elevations occur, which are lymph-ganglia, and have been erroneously termed "follicular glands." They are accumulations of lymph-tissue with numerous follicular formations, and in their centers usually show a longitudinal cleft, in open communication with the outer surface of the tongue. Stratified epithelium directly covers the lymph-ganglion, the papillæ being imperfectly developed on the outer periphery of the ganglion and altogether wanting within the cleft. Sometimes the fibrous connective tissue produces a distinct capsule around the ganglion. Diffused layers of lymph-tissue immediately above the muscle of the tongue are also observed, especially in children.

The muscle-fibers of the tongue are of the striped variety; they interlace in different directions and produce a dense felt-work, are attached to the fibrous septum in the longitudinal median line of the tongue, and freely ramify upon approaching the mucous layer, with which they blend. The perimysium contains a varying number of fat-globules, chiefly in the posterior portions of the tongue.

The blood- and lymph-vessels are numerous. The latter, according to Teichmann, produce two plexiform extensions, the upper and finer of which lies close beneath the papillæ, receiving the usually single lymph-ramules from the filiform papillæ and the plexuses from the fungiform and circumvallate papillæ. Rich plexuses of lymphatics surround the lymph-ganglia.

(3) *In the pharynx and œsophagus* the structure of the mucosa resembles that of the oral cavity — *i. e.*, it has small papillæ, not distinctly marked on the epithelial surface. The latter is stratified and produces small acinous mucous glands, which are more numerous in the throat than in the œsophagus. In the lower half of the œsophagus they are absent, except in the portion immediately above the cardiac orifice of the stomach (Kölliker). The stratified epithelial investment in the neighborhood of the choanæ blends with the ciliated columnar epithelia of the nasal cavities.

The lymph-tissue is a widely spread formation in the mucosa of the pharynx; besides, a large amount is stored up in the two lymph-ganglia, *the tonsils*, which are situated in the niches

between the glosso-palateal and pharyngo-palateal folds. The tonsils vary greatly in size; sometimes the lymph-follicles which build them up are scanty, at other times numerous. From the covering mucosa a number of depressions are formed, similar to those of the lymph-follicles on the base of the tongue. These depressions in the tonsil may have several lateral elongations uniting with a central cleft, the so-called crypts of the tonsil. In the cavities a viscid, cheesy mass is often formed, which is not infrequently the seat of a calcareous deposition. The mass proves upon examination to be composed of leptothrix (E. Grüning), a fungus which is a normal occurrence in all furrows of the oral cavity, especially those between the gums and the teeth. In the mucosa covering the tonsils, acinous mucous glands are present. Hyperplastic tonsils do not histologically differ from normal lymph-ganglia, with numerous follicles.

In various situations in the wall of the pharynx lymph-tissue is found, and on the roof the aggregation of this tissue bears the superfluous name of the pharyngeal tonsil.

The *œsophagus* in rest appears completely closed by large folds of the mucosa, which is composed of a loose fibrous connective tissue, and admits of a high degree of extension. Along the epithelial cover it shows numerous small papillæ, but which are not marked on the surface of the stratified epithelium. The vascular supply is very abundant in the layers, directly below the epithelium, but scanty in the portion near the muscle. The muscle in the upper half or two-thirds of the œsophagus is of the striated variety, composed of at least two layers, an outer longitudinal and an inner circular, and in some places near the mucosa a second longitudinal or oblique layer is often found. In the œsophagus of the rabbit this is a constant formation. (See Fig. 251.) In the lower portions of the œsophagus a gradual transition of the striated into smooth muscle-fibers takes place. In the posterior wall, according to Treitz, the striped muscles extend down more deeply than in the anterior, and bundles of these muscles terminate in tendinous formations, which blend with the external fibrous investment. The mucosa of the œsophagus has also independent bundles of smooth muscle-fibers, which are scanty in its upper portions, but form a continuous layer in the thoracic portion (Toldt).

(4) *The Stomach.* The mucous layer of the stomach is marked by an abundant glandular apparatus, the so-called *gastric tubules* or *pepsine glands.* This mucosa, owing to its attachment to the

muscle-layers, is capable of producing very large folds, which are arranged longitudinally from the cardia to the pylorus, and are least marked in the latter situation. When the stomach is empty, the folds of the mucosa completely occlude the cavity. The covering surface epithelium of the stomach is indistinctly stratified; the innermost flat, horny layer and the columnar layer are well marked, while the middle layers of cuboidal epithelia are often wanting. The difficulty of obtaining for examination the unchanged gastric mucosa of man is, perhaps, the reason why the presence of flat, horny epithelia has been overlooked. The columnar epithelium gradually loses its character,

FIG. 251.—ŒSOPHAGUS OF A RABBIT. TRANSVERSE SECTION.

E, horny layer, *R*, rete mucosum, *C*, layer of columnar epithelia; *M*, loose connective tissue, with injected blood-vessels; *T*, circular layer of striped muscles, with the adjacent oblique and longitudinal layers, *L*, *L*[1]. Magnified 150 diameters.

and is transformed into the cuboidal epithelium of the gastric glands.

The majority of the *gastric glands* are of the simple tubular variety, though it often happens that two or more tubules empty into a common tube of larger caliber, opening at the inner surface of the mucosa. In the stomach of man, in the middle portions of the mucosa, branching tubular glands are said to occur (Kölliker).

Such an appearance is sometimes produced by tubules which run obliquely or in a winding course, which in vertical sections seem to inosculate with the perpendicular tubules. The gastric glands are lined with cuboidal epithelium, with interspersed formations of large, pale, finely granular epithelia, to the presence of which R. Heidenhain and A. Rollet drew attention. The Greek denominations given to them by the last-named observer are superfluous in the face of the fact that the difference in the appearance of the epithelia is due simply to the process of secretion. The coarsely granular, indistinctly nucleated, epithelia are for the time being not engaged in the production of the mucous secretion termed pepsine; while the large, pale, distinctly nucleated epithelia are laden with it. Pepsine consists, in part, at least, of transformed living matter of the epithelia. By an accumulation of liquid the bioplasson reticulum is at first stretched, afterward torn, and large portions of the bioplasson perish in the formation of pepsine. By the rupture of the cement investment, the secretion is discharged into the caliber of the tubule. As the glandular epithelium forms only one layer, the swelled epithelia bound the caliber in the same manner as the ordinary cuboidal ones, and it is only in a surface section of the tubule that the swelled epithelia appear near the basement layer of the connective tissue, as if covered by coarsely granular cuboidal epithelia. These relations are most definitely marked in places where the same tubule is, owing to its winding course, seen in longitudinal and transverse directions. (See Fig. 252.)

FIG. 252.—GASTRIC GLANDS FROM THE STOMACH OF MAN. VERTICAL SECTION.

L, tubule in a longitudinal; *T*, tubule in a transverse section, lined by cuboidal epithelia; *P*, epithelia laden with pepsine. Magnified 800 diameters.

The secretion of the tubular glands—the gastric juice—owes its acidity to the presence of a small quantity of hydrochloric acid. This reaction is obviously induced through the agency of

the epithelia themselves, which obtain their material from the alkaline blood. It should be borne in mind that gastric juice is a product of living matter, and as such is beyond the reach of chemical analysis. Chemists have tried in vain, so far, to explain the production of gastric juice by complicated formulæ and ingenious calculations. The large number of Greek names given to the artificial products in the chemist's retorts sufficiently proves their want of knowledge in this matter. The solution of the puzzle, why the acid gastric juice does not digest the wall of the stomach itself, has also occupied speculative minds to a considerable extent, but no satisfactory answer has as yet been obtained.

The delicate fibrous connective tissue between the tubular glands forms a basement layer, which furnishes support for the epithelia, and carries the blood-vessels, which are very numerous in the mucosa of the stomach. The vascular plexus woven around the tubules is extremely dense, and near the surface of the mucosa composed of wide capillaries. (See Fig. 253.)

In transverse sections of the pepsine glands, in which the central calibers of the tubules are best marked, the vascular plexus is seen surrounding the tubules, and, if injected with colored gelatine, many of the capillaries appear to be almost in contact with the base of the epithelial wreath. In such sections the relation between the empty and the laden epithelia is also marked; in the portion nearest the central caliber the latter are partly overlapped by the former. (See Fig. 254.)

FIG. 253.—MUCOSA OF THE STOMACH OF A RABBIT. VERTICAL SECTION.

F, layer of horny epithelia; E, cuboidal epithelia, P, epithelia laden with pepsine. The delicate connective tissue between the tubular glands containing injected blood-vessels; A, artery; V V, veins; M, smooth muscle-layer of the mucosa. Magnified 300 diameters.

The tubular formations toward the pylorus have been described as being mucous glands, without any decided anatomical

proof; here acinous mucous glands begin to appear, blending with those of the duodenum.

The connective tissue of the mucosa of the stomach, especially in children, is composed largely of the myxomatous variety and abundantly supplied with lymph-corpuscles. Both in the fundus and the pyloric portion of the stomach of man lymph-tissue appears as follicles and groups of follicles, which by mistake have been termed "lenticular glands." Their number, however, varies greatly, and in the localities where they exist pepsine glands are not found.

The mucosa of the stomach has a nearly continuous layer of smooth muscle-fibers, composed of circular and longitudinal bundles; the circular fibers send prolongations between the tubular glands.

The muscle-layers of the stomach proper are of considerable width, and principally arranged in two layers—an inner circular and an outer longitudinal; the bundles of both being freely interlaced with oblique bundles. The circular layer produces the sphincter-muscle of the pylorus.

FIG. 254.—MUCOSA OF THE STOMACH OF A RABBIT. HORIZONTAL SECTION.

E, cuboidal epithelia of the tubular glands; *P*, epithelia laden with pepsine, *C*, connective tissue between the tubules, containing injected blood-vessels. Magnified 300 diameters.

(5) *The Small Intestine.* In transverse sections of the small intestine the layers constituting its wall appear as follows: *(a)* the *mucosa*, producing reduplications above the level of the inner surface, the *villi*, and reduplications below the level of the inner surface, the tubular *intestinal glands*; *(b)* the *submucous layer*, holding circular and longitudinal layers of smooth muscle-fibers, and a varying amount of lymph-tissue (the so-called adenoid tissue); *(c)* the *muscle of the intestine proper*, composed of a broad circular and a narrow longitudinal layer of smooth muscle-fibers; and *(d)* the covering *peritoneum*. (See Fig. 255.)

The *villi* are reduplications of the mucosa, of a conical or cylindrical shape, very long and narrow in portions where the muscle of the intestine is contracted; broad and short, on the contrary, where the muscle of the intestine is extended. In the highest degrees of distension (by gaseous material) the inner

surface of the mucosa is smooth, and no villi are perceptible. Each villus comprises the following layers: *(a) a covering columnar epithelium ; (b) myxomatous connective tissue*, forming the central portion of the villus; in this are imbedded *(c)* delicate *longitudinal* (Brücke) and *transverse* (Moleschott) bundles of smooth muscle-fibers; *(d)* a rich plexus of *capillary blood-vessels*, and *(e)* a central *lymph* or *chyliferous vessel.*

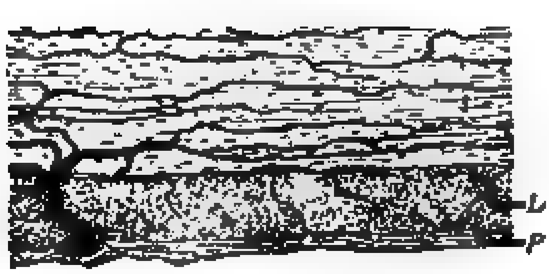


FIG. 255.—SMALL INTESTINE OF A DOG. TRANSVERSE SECTION. BLOOD-VESSELS INJECTED.

V, villi. *G*, tubular intestinal glands; *M*, longitudinal muscle-layer of the mucosa. *A*, lymphatic (adenoid) or submucous layer; *R*, circular muscle of the intestine, cut longitudinally, *L*, longitudinal muscle of the intestine, cut transversely. *P*, peritoneum. Magnified 25 diameters.

The epithelium is of the columnar variety, with numerous wedges or intercalated formations between the conical or cylindrical bodies. These are separated from each other by an envelope of cement-substance, which is traversed by connecting filaments (see page 130, Fig. 44). The cement-substance is well developed on the free surface of the epithelia, producing the so-called "basal seam" of authors. This seam consists of a thin and homogeneous layer of cement-substance, studded with a number of short, delicate rods, which are plainly visible only when, by imbibition of a liquid, the epithelium is slightly swelled. To the presence of these rods Brettauer and Steinach first drew attention, while Kölliker and Funke considered the vertical striation of the basal seam to be minute pore-canals. According to the difference of conception as to the structure of the seam, some physiologists claim that the finest fat-granules,

during the process of absorption, are taken into the epithelia *between* the rods, while others maintain that the *rods themselves* take up the fat-granules. Above the columnar epithelia flat endothelial formations have been described, constituting the outermost investment of the connective tissue (Watney, Krause, Debove).

The manner in which liquids are taken up into the blood- and lymph-vessels of the villus is by the active participation of the columnar epithelia (Spina). During absorption, especially shortly after fatty food has been eaten, the interior of the villi and also of

FIG. 256.—VILLUS FROM THE SMALL INTESTINE OF A CAT. VERTICAL SECTION. [PUBLISHED IN 1868.]

A, myxomatous (so-called adenoid) tissue; in its center the lymph-vessel, bounded by smooth muscle-fibers and filled with fat-granules; *F*, cleft between the columnar epithelia, in connection with the central lymph-vessel. Magnified 800 diameters.

the covering epithelium is found to contain a large quantity of fat-granules of different sizes, and the conclusion arrived at by Gruby and Delafond was that the fat-granules were first taken up by the epithelia, which convey them into the interior of the villus. Since that time, most of the physiologists have attempted to explain the absorption of fat from the basal surface of the epithelia; but the whole process is as yet an unsolved puzzle. We

could understand the penetration of fat-granules between or into the rods, but how the horny and apparently solid layer of cement-substance, serving as a base for the implantation of the rods, could be penetrated by fat-granules is not intelligible.

In 1868 I published the results of my researches during a whole year (*l. c.*, see page 401). I drew attention to the fact that in specimens of uninjured villi, independently of furrows produced by contraction, the apices look as if split, often giving exit to a mucous mass, or a portion of myxomatous tissue of the villus, and that in true vertical sections of the villi there are gaps seen between the epithelia which are in direct connection with

C

C

B

FIG. 257.—VILLUS FROM THE SMALL INTESTINE OF A GUINEA-PIG. FRESH SPECIMEN. [PUBLISHED IN 1868.]

V, vacuole in the columnar epithelium; *CV*, granular (chlorophyll?) corpuscle in a vacuole; *C*, granular (chlorophyll?) corpuscles in the myxomatous tissue; *B*, capillary blood-vessel. Magnified 800 diameters.

the central lymph-vessel, as proved, especially when both are filled with fat-granules. (See Fig. 256.) Whenever colored liquids are injected into the lymphatics of the small intestine (before injecting the blood-vessels), it has long been known that the colored mass escapes through the apices of the villi into the intestinal canal. I have examined the small intestines of sixty-eight guinea-pigs, and found, in a large majority of the villi of

these animals, peculiar granular bodies, usually accumulated along the apices, but occurring also in the vacuoles of the epithelia, or in goblet-like formations produced by the epithelia. A few guinea-pigs which I examined in New-York exhibited the same formations—formations that do not occur in the intestines of other herbivorous animals I had examined. These are clusters composed of a pale granular mass, containing a number of green or greenish-yellow granules, with a high degree of refraction; I also found isolated granules of various sizes. (See Fig. 257.)

The differences in the number, the color, and appearance of these bodies were found to vary according to the following conditions: Embryos of guinea-pigs, examined a few days before birth, had no corpuscles in their villi. Newly born guinea-pigs, one to two hours after birth, showed no corpuscles; but sixteen to twenty-four hours after birth, the animals being fed with oats, the villi showed a number of yellowish-green bodies, with fine granules. All the animals of a more advanced age exhibited the green corpuscles in the villi. The color was evidently dependent on the vegetable food. After feeding with fresh blades of grass a light chlorophyll-green was seen, and a light, pure yellow color appeared after feeding with the flowers of *leontodon taraxacum;* a dim yellowish-green was observed after a continued administration of vegetables. When the stomach remained filled with food the contents, from the cardia toward the pylorus, showed all shades of green to yellow-green; this green shade remained for a month or a month and a half after the fresh vegetable diet had been stopped and amylaceous food had been exclusively administered. A light yellow-green color was mainly observed in autumn and after feeding with straw. If blue aniline was mixed with the food the granules assumed a dark bluish-green. After administration of starchy food for one and a half to two months, the granules were colorless and the animals died, evidently from starvation; it was only under these conditions that the stomach was found empty. The granules were largest after feeding with the young leaves of plants, and smallest after administration of dry vegetable food or oats. The age of the animals had no influence upon the color and shape of the granules. In two instances I found such granules in mesenteric ganglia also.

Unquestionably the granules are chlorophyll granules, and their coloring matter is chlorophyll; for it can be extracted with alcohol, and assumes a yellowish-brown color when preserved in chromic acid. Very probably these bodies are vegetable bioplasson, having left the shell of cellulose. But in what way did they penetrate into the stroma or central lymph-vessel of the villus?

In guinea-pigs several hours old I found villi containing three or four corpuscles in their axes, the uppermost of which was located in a crateriform depression in the middle of the apex. Not

infrequently the central canal contained only a row of these corpuscles, as proved by vertical sections through villi, in specimens hardened in a solution of chromic acid. Sometimes in fresh specimens the green bodies were seen, as if incarcerated at the apex in an intra-epithelial canal. By gentle pressure on the covering-glass some of the bodies could be forced out from the apex (see Fig. 258). From these phenomena in the small

FIG. 258.—VILLUS FROM THE SMALL INTESTINE OF A GUINEA-PIG. FRESH SPECIMEN. [PUBLISHED IN 1868.]

C, granular (chlorophyll?) corpuscle, forced out from the interior of the villus. *O*, such corpuscles filling the cleft between the columnar epithelia. *B*, capillary blood-vessel. Magnified 800 diameters.

intestine of guinea-pigs, from anatomical facts, and a number of successful experiments in bringing extraneous matters (carmine and aniline granules) into the lymph-vessel of the villus from without, it would follow that the apex of the villus has in its epithelial investment one or two perforations in direct connection with the central lymph-vessel, which serves to take up solid material, mainly fat-granules. J. Nath. Lieberkühn, in 1745,

described "ampullæ" in the villi, which, by some physiologists, were considered to be widenings of the chyliferous vessel at the base of the villus. *I have made the presence of such openings certainly probable, even though positive proofs of their existence are still wanting.*

Along the epithelial investment of the villi goblet-like formations are often seen, more numerous in animals having an increased mucous discharge from the intestine — *i. e.*, diarrhœa. In 1868 I maintained that these formations were the shells of cement-substance, after the contents — the mucus — had been emptied out. This theory was contrary to the ideas of some observers, who claimed that the goblets had been artificially produced, or were specific secretory organs. Donders and Kölliker had, previously to the publication of my views, described these formations as connected with the secretion of mucus, and this idea proved to be correct.

The epithelial investment of the mucosa of the intestine forms tubular glands, the *intestinal glands* or so-called *crypts of Lieberkühn*, which are located beneath the level of the mucosa, and, being more numerous than the villi, empty by minute openings around the base of the villus. Their lining epithelium is columnar, exhibiting the same basal seams as those covering the villi. The intestinal glands are absent in localities where lymph-follicles are imbedded in the mucosa.

The mucosa of the duodenum, chiefly in its upper third, holds *racemose glands*, which are situated below the level of the lower extremities of the intestinal glands; these are called Brunner's glands, and their secretion is considered to be mucus. In the descending portion of the duodenum they gradually become scantier, and especially so below the openings of the bile-duct.

The mucosa of the small intestine is supplied with a *double layer of smooth muscle-fibers*, independent of the muscle-layers of the intestine itself. The innermost is circular, running between the tubules and penetrating through vertical prolongations the myxomatous structure of the villi, where several delicate bundles are formed by it; the outer muscle-layer is longitudinal, being in most localities decidedly broader than the circular layer. Transverse sections of portions of the small intestines, hardened by having been placed in a solution of chromic acid immediately after the animal's death, plainly show that where the muscle of the intestine is broad, consequently contracted, and the caliber of the intestine narrow, the villi are elongated and thread-like or

cylindrical in shape; while, where the muscle is extended, the villi are seen as conical or blunt elevations. The villi corresponding to the place of attachment of the mesentery are always the smallest, those on the opposite surface the largest. The lobate form of the short conical villi is due to the contraction of the bundles of smooth muscle-fibers contained in the myxomatous stroma of the villus, as first intimated by Brücke. In 1868 I concluded, therefore, that the shape of the villi of the intestine is not fixed, but varies between that of a cylinder and that of a cone, depending on the contraction or extension of the intestinal tube, the peristaltic motion thus producing a continuous change. I also concluded that the muscle-layers of the intestine proper are antagonistic in their action to the muscle-layers of the mucosa; in other words, when the muscle of the intestine is in the highest degree of contraction, the muscles of the villi, being prolongations of the muscle of the mucosa, are extended, and *vice versâ*. An extended villus has a smooth surface; the lobation begins as the villus changes its shape from the cylindrical to the conical. In the extended condition of the villi,—*i. e.*, when the muscle of the intestine is contracted,—the presumed openings at the apices of the villi are gaping and ready to absorb the fat which is present as an emulsion in the considerably narrowed caliber of the intestine, and reduced to extremely small granules, perhaps, by the mechanical action of the rods of the basal seam of the epithelia. As soon as the contraction of the muscle of the intestine ceases, the contraction of the muscle of the mucosa sets in, the villi become retracted, and the openings at their apices closed. By this process the absorbed fat will be carried backward into the lymphatic or chyliferous system. Probably there is also an antagonism between the circular and longitudinal layers, both of the mucosa and the intestine.

The mucosa of the intestine immediately above the muscle is abundantly supplied with lymph (so-called adenoid) tissue, which produces a continuous layer and is accumulated in the solitary follicles and in groups of the aggregated follicles—the so-called Peyer's patches. E. Brücke first drew attention to the lymphatic nature of these formations. The solitary follicles appear to the naked eye as flattened protrusions above the level of the mucosa, or as bare spots, or even as shallow depressions. The columnar epithelium covering the surface of the follicle is shorter than the epithelium covering the villi. Villi are wanting in those parts of the mucosa which are furnished with solitary

follicles and patches; the tubular intestinal glands within the territory of a follicle may be either absent or present only in small numbers. In the contracted portions of the intestine, the follicle, protruding as a conical elevation, is overlapped by the surrounding villi; while in the extended portions the follicle is flattened and the villi stand at a certain distance around it. The longitudinal layer of the muscle of the mucosa is perforated, corresponding with the extent of the follicle, and surrounds its periphery. (See Fig. 259.)

FIG. 259.—SMALL INTESTINE OF A RABBIT. VERTICAL SECTION IN THE LONGITUDINAL AXIS. LYMPH-VESSELS INJECTED.

V, villi; *MM*, longitudinal muscle-layer of the mucosa, *F*, lymph-follicle; *M*, fibrous connective tissue; *T*, circular muscle of the intestine, in transverse section; *L*, longitudinal muscle of the intestine, in longitudinal section; *P*, peritoneum. Magnified 25 diameters.

(6) *The large intestine* is similar in structure to the small, but destitute of villi; its mucosa, being of a myxomatous character, shows elevations and folds arranged in a circular direction. The tubular intestinal glands are larger than in the small intestine. The lymph-tissue is either distributed uniformly in the submucous layers, or is accumulated in the follicles, which are, it is

maintained, in no way connected with the chyliferous vessels. The submucous portion of the vermiform appendage has a very broad layer of lymph-tissue. While the muscle of the small intestine is almost uniformly distributed throughout the tube, and the circular always shows greater development than the longitudinal; in the large intestine, on the contrary, the outermost longitudinal muscle-layer is imperfectly developed, but in certain places, called *tæniæ*, accumulates in ribbons. At the point of the junction of the ileum and coecum the circular muscle-layer enters the formation of the valvula Bauhini, while the longitudinal layer directly passes from the small to the large intestine.

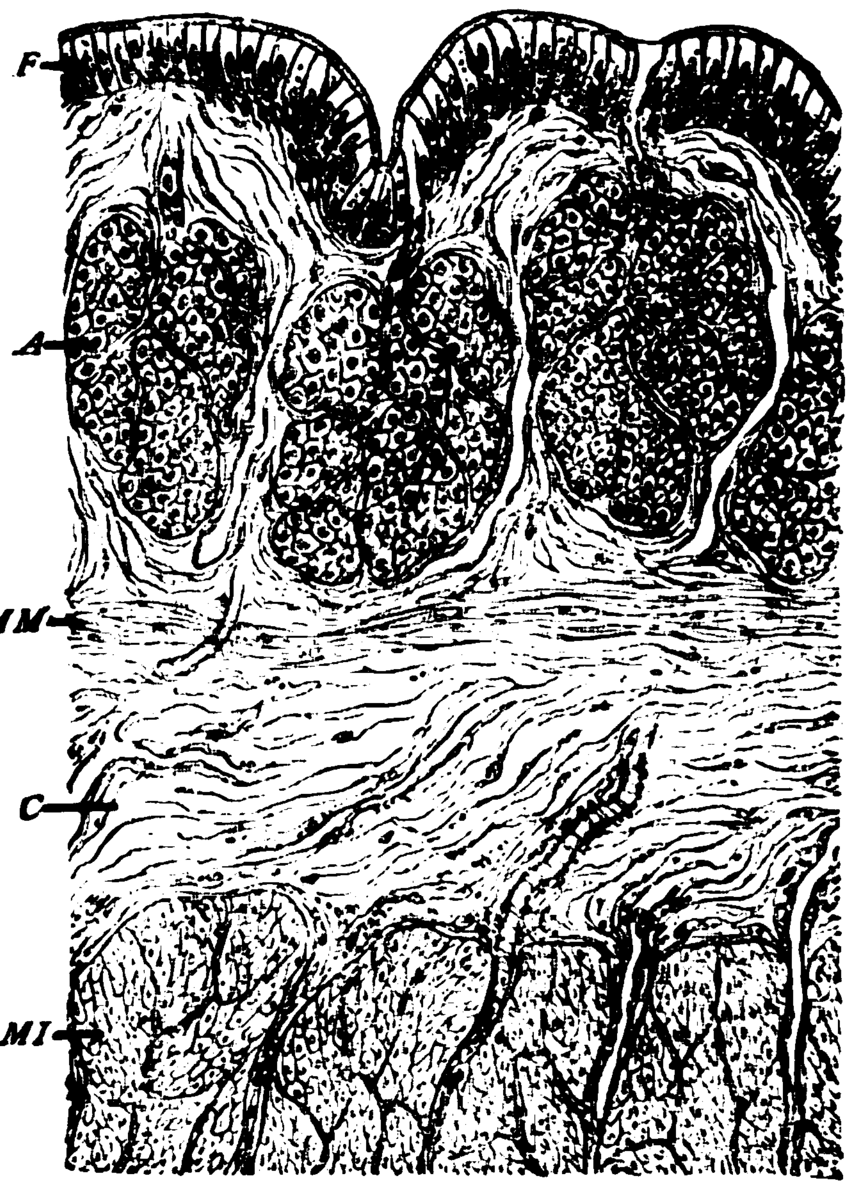


FIG. 260.—RECTUM OF A DOG. VERTICAL SECTION IN THE LONGITUDINAL AXIS.

F, columnar epithelium; *A*, acinous mucous glands; *MM*, longitudinal muscle-layer of the mucosa; *C*, submucous fibrous connective tissue; *MI*, circular muscle of the intestine, in transverse section. Magnified 300 diameters.

The mucosa of the rectum exhibits reduplications like that of the large intestine, and is, in its lower portions, supplied with a varying number of racemose glands, especially well developed in the rectum of the dog. (See Fig. 260.) The internal sphincter is constituted by an aggregation of the smooth circular muscle-fibers, while the external sphincter is composed of striated mus-

cle-fibers in a circular and plexiform arrangement. Both circular and longitudinal layers are uniformly distributed throughout the wall of the rectum, attaining their greatest width near the anus. The transition of smooth to striped muscle-fibers is gradual.

Blood-vessels of the Intestines. According to C. Toldt, the distribution of the blood-vessels in the intestines closely resembles that of the stomach, their arrangement being nearly identical in the stomach and the large intestine. The *arterioles* send branches to the peritoneum and pierce the longitudinal muscle-layer, between which a further division takes place by the formation of elongated capillary meshes, for the supply of the two muscle-layers of the intestine proper. After having perforated the circular muscle,—always, of course, in the external perimysium which separates the larger muscle-bundles,—the arterioles reach the submucous layer, producing, by repeated bifurcations and anastomoses, an extended vascular plexus. Finally, the arterioles penetrate the longitudinal muscle-layer of the mucosa and form the terminal arterial plexuses extended beneath the tubular glands, from which arise the terminal arterioles for the supply of the uppermost portions of the mucosa. In the stomach and the large intestine the capillaries are woven around the tubular glands, and widen beneath the surface epithelium to double their original diameters in circular loops around the openings of the tubules. From these superficial capillaries arise the veins, which, at regular intervals, pass downward between the glands and empty into venous plexuses within the mucosa. The efferent veins arising from this plexus accompany the arteries downward. In the small intestine the arterioles penetrate the myxomatous tissue of the villi; each villus contains one or two arterioles, which branch very freely into capillaries. The latter are in connection with the capillaries of the tubular glands. The veins originate at the apices of the villi from slightly widened capillaries. (See Fig. 255.) In the duodenum the acinous glands are supplied with capillaries of their own, and so are all lymph-follicles of the small and large intestine.

The *lymph-vessels of the intestines* produce a separate capillary plexus for the muscle-layers and for the mucosa. The former was first described by Auerbach, who found that the lymphatics collect into the so-called interlaminar lymphatic reticulum, located between the longitudinal and circular muscle-layers. Flat plexiform extensions of lymphatics exist in the submucous layer

beneath, and in the mucous layer above, the longitudinal muscle of the mucosa, the latter plexus being situated at the bottom of the tubular glands; both are connected by oblique branches piercing the muscle-layer. The lymphatics arising from the submucous layer are supplied with valves; they leave the intestine at the insertion of the mesentery. The connective tissue of the peritoneum possesses a lymphatic capillary system of its own, producing the so-called subserous plexus. The lymphatics form sinuses around the gastric glands (Lovèn), a number of which are included between two lymphatics. The uppermost sub-epithelial lymphatics are plexiform, or originate as pointed tubules. Similar relations are found to exist in the large intestine. In the small intestine the beginnings of the lymphatics are found in the central portions of the villi, either as a wide, single tubule or as two or more longitudinal tubules with transverse connections. Even single tubules may, at the apex, produce a loop, from which, in injected specimens, pointed prolongations between the epithelia are often seen arising. (See Fig. 259.) The lymphatic or chyliferous vessels of the villi have a complete lining of endothelia. A closed reticulum of lymphatics surrounds the lymph-follicles, though it is generally believed that, in the rabbit's intestine, the follicles are encircled by a sinus.

The *nerves of the intestines* are of both the medullated and non-medullated varieties. They form a plexus above the peritoneum, and, after having traversed the longitudinal muscle-layer, give rise to the plexus between the longitudinal and transverse muscle-layers (Auerbach's plexus), which is composed of reticular extensions of nerves, with numerous interspersed ganglionic nerve elements. From the nodular ganglia of this plexus numerous non-medullated nerve fibrillæ emanate for the supply of both muscle-layers. A number of nerve-fibers pass through the perimysium of the circular muscle to the submucous layer, where again a plexiform extension is produced, with interspersed ganglionic elements (Meissner's plexus). Its nerve branches supply the mucosa and the muscles of the mucosa. The globular or oblong ganglionic elements are decidedly larger in the submucous than in the intermuscular plexus. (See Fig. 261.) In what manner the ultimate nerve fibrillæ terminate is not known.

(7) *The salivary glands* are large racemose glands which secrete a watery or mucous liquid, and empty either into the oral cavity (the parotid, submaxillary, and sublingual glands), or into the duodenum (the pancreas). According to A. Heiden-

hain and Lavdowsky, there are glandular formations of the racemose variety, such as those found in the nasal mucosa, which are called *serous glands*, and which produce a watery secretion. The parotid gland and the pancreas may also be grouped with this variety. Others — the sublingual gland — discharge a mucous, viscid liquid, while the secretion of the submaxillary is partly serous and partly mucous. The differences in the appearance of the glandular epithelia may be understood when we recall the process of mucous secretion in general. (See page 329.) Epithelia not participating in the process of secretion are

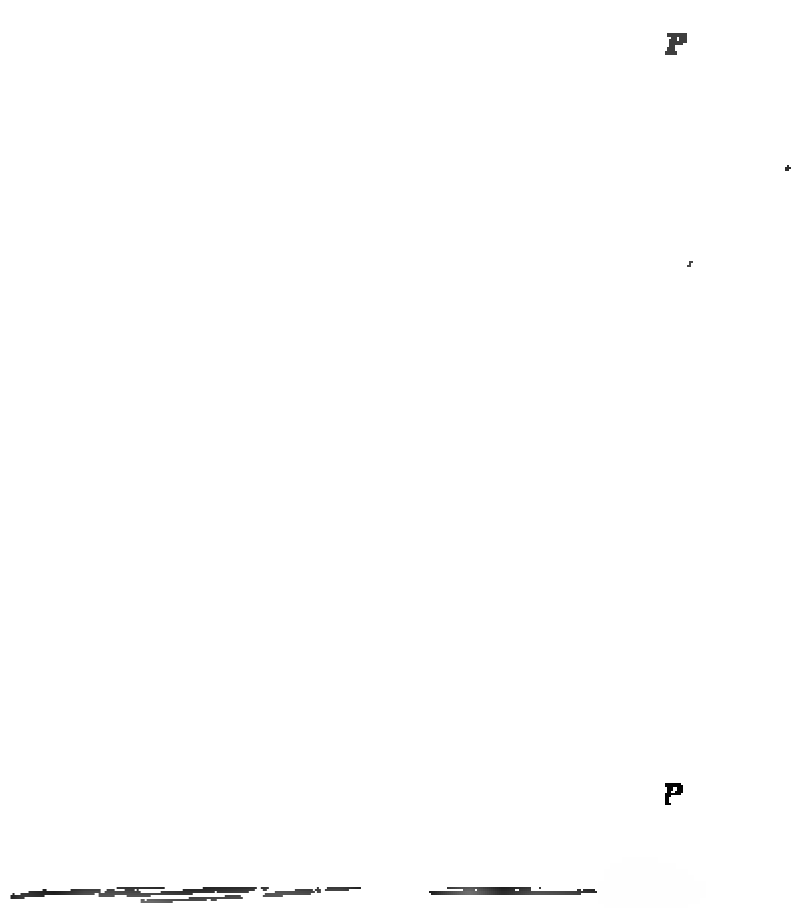


FIG. 261.—NERVE-PLEXUS OF THE SMALL INTESTINE OF A CAT.

M.P. Meissner's plexus; *S*, submucous fibrous connective tissue; *T*, circular muscle of the intestine, in transverse section; *A.P.* Auerbach's plexus; *L*, longitudinal muscle of the intestine, in longitudinal section. Magnified 600 diameters.

found, according to R. Heidenhain, immediately beneath the structureless layer, and are termed by him the bordering cells, being the reserve from which epithelia are supplied to take the place of those which were destroyed by the secretion of mucus. Such reserved epithelia are not found in serous glands — for instance, in the parotid. Different portions of the submaxillary gland exhibit both varieties of the epithelia, which blend with

each other. The pancreas has the smallest acini, and here the epithelia are found coarsely granular, even homogeneous toward the structureless layer. Some observers have erroneously claimed that this gland belongs to the tubular variety. The ducts of all salivary glands are lined by columnar epithelia. The pancreatic duct is provided with acinous mucous glands. The columnar epithelia, in the smaller ducts chiefly, show a delicate longitudinal striation, which is most distinctly marked in the portion of the epithelium nearest the structureless layer. The significance of this striation will be dwelt upon in the article by H. B. Millard, treating of the epithelia of the kidney. In the tubules of the ducts inosculating with the acini, the epithelial lining shows slight differences in different salivary glands.

Saliva, transferred to the slide in a perfectly fresh condition, and covered with a thin covering-glass, is an excellent specimen for the study of bioplasson bodies. Besides flat epithelia from the oral cavity and a varying number of leptothrix, we find the *salivary corpuscles* — *i. e.*, the former tenants of glandular epithelia. These are nucleated plastids exhibiting the reticular structure and amœboid movements, at usually the ordinary temperature of the room. To study the form changes, it is advisable to sketch on paper from the beginning of the investigation. Large, swelled corpuscles, with pale, vesicular nuclei, may also be found, containing granules which, being the remnants of the torn reticulum, are in an active so-called "molecular" motion. The number of such hydropic corpuscles increases with the duration of the observation under the microscope. At last both the active and hydropic corpuscles burst, and masses of detritus or clusters of granules result. The nuclei of the flat oral epithelia also exhibit the reticular bioplasson structure, and are obviously endowed with vitality, which endures for some time after the horny change of the rest of the epithelium has taken place (Stricker).

In *thrush* (see page 44), the whitish patches consist of an aggregation of leptothrix, oïdia, and scanty-chambered mycelia; in short, the constituent elements of mildew.

In *catarrhal stomatitis*, the number of salivary corpuscles is considerably augmented, and the amount of the bioplasson they contain increased, as shown by their coarser granulation. Such corpuscles attain all the appearances of pus-corpuscles, and may be so termed. Stringy threads of mucus are also found in even slight degrees of inflammation of the mucosa, caused by mucous transformation of bioplasson before its ejection from the epithelia, and coalescence of a number of mucous globules. A small amount of blood is usually found intermixed.

In *croupous inflammation*, the grayish white, so-called "pseudo-membranous" formations covering the swelled and considerably hyperæmic mucosa, consist of a fibrinous exudation, which under the microscope appears as a felt-work of sometimes narrow, sometimes broad, granular fibrils. (Represented on page 516, Fig. 212.) In the meshes of this irregular felt-work scanty bioplasson bodies are found, which may be considered either as nuclei of former epithelia, destroyed in the production of the croupous exudate, or as

emigrated colorless blood-corpuscles (so-called "leucocytes"). The determination as to the particular source of these corpuscles, in the present condition of our knowledge, is impossible. The *diphtheritic exudation* is of exactly the same character as the croupous; its nature is determined by its deep site in the tissue of the mucosa, and is often recognizable under the microscope by the presence of isolated globular clusters of lymphatic (adenoid) tissue, from which putrefaction starts. The globular nests filled with micrococci originate from such clusters of lymphatic tissue.

XVI.

THE TEETH.

EVERY tooth in the socket of the jaw is in close connection with the surrounding structures and is composed of living tissues. Morbid processes, especially caries, produce more or less painful sensations in the tooth, even before the pulp-cavity has been invaded. The cutting with dental instruments of healthy portions of the tooth is an unpleasant and even painful process to the patient, and especially so at the boundary between the enamel and the dentine, and in the neck of the tooth. Foreign bodies, such as fillings of any description, if brought in contact with dental tissues, set up an inflammatory condition, resulting in the so-called "consolidation" of dentine—a process which, a century ago, was observed by Göthe in the dentine of the elephant's tusk after a bullet had been accidentally driven into this tissue. The sensation called "putting the teeth on edge," caused by eating sour fruits, is another proof of the presence of life in the tooth. All former observers, however,—though some of them have maintained the presence of nerves in the dentine,—failed in demonstrating the living matter in its most intricate distribution, partly owing to the faulty method applied for microscopic research, and partly to the lack of knowledge in the arrangement of living matter in other and kindred tissues of the body. Dry specimens, formerly resorted to, are only mummies in which a frame of lime-salts is left, but the soft parts—the seats of life—have disappeared. Our present knowledge of the minute anatomy of the teeth, as displayed in the following articles, is largely due to the improved methods applied for research.

DENTINE, CEMENT, AND ENAMEL. BY C. F. W. BÖDECKER, D. D. S., M. D. S.*

Methods. The best method for preparation of bone-tissue for microscopical purposes is doubtless the treatment with chromic acid solution of the strength of a half to one per cent. The same treatment has repeatedly been resorted to by different investigators of tooth-substance. I have used this solution extensively for this purpose, with precautions suggested by the experience on bone. These are: to immerse only a few teeth in a large vessel with a considerable amount of chromic acid solution; to renew the same every third or fourth day, and add, to enforce the action of the fluid, very small quantities of dilute hydrochloric acid. By this treatment the teeth, after a few months, become dark green from the reduction of the chromic acid to the sesquioxide of chromium. This method is doubtless the best for softening teeth, although the chromic acid softens the cement and dentine only to a certain depth, so that a tooth kept in the chromic acid solution never is fit to be cut through in its whole substance at one time. The sections so obtained are ready for staining with carmine or hæmatoxylon, and after they have been immersed in and washed with distilled water, also for staining with chloride of gold.

The greatest objection to the chromic acid treatment is that enamel never can be obtained in connection with the dentine. If hydrochloric acid has been used, in addition to the chromic acid solution, the enamel is almost completely dissolved. If chromic acid alone has been used, the enamel becomes so brittle that it crumbles into small particles under the knife.

Lactic acid acts upon teeth, if diluted sufficiently, by dissolving the lime-salts much faster than chromic acid. Specimens prepared in this way, however, in my experience, are not distinct enough for study with high powers.

The only method which enabled me to obtain specimens of teeth provided with all hard tissues is the following: A fresh tooth, or one kept a short time in chromic acid solution, is sliced under water by a watch-spring saw, and ground as thin as possible upon a corundum-wheel of a lathe, always being kept under water. The lamella thus obtained should be placed in a large quantity of chromic acid solution, of the strength of half of one per cent., for one or two days, with the view of hardening the soft parts of the tooth and dissolving the lime-salts. After this the specimen may be stained with carmine, hæmatoxylon, chloride of gold, etc., as above described, and mounted in dilute glycerine. The saturated solution of picric acid in water may also be used for the decalcification of a ground slice of a tooth.

Dentine. We know that the basis-substance or matrix of the dentine is analogous to that of bone, viz.: glue-yielding, and at the same time infiltrated with lime-salts. We learned from the researches of E. Neumann that the basis-substance is denser on the walls of the tubuli, and more resistant to the action of strong acids, which cause the appearance of a sheath around each tubule after the solution of the intermediate substance of the matrix between the tubuli.

With low powers we cannot see in the dentine anything but the tubuli, which I propose to term hereafter *dentinal canaliculi.* These, as is well known, run in curved sigmoidal lines from the boundary of the pulp-cavity to the periphery of the dentine; they are directed obliquely upward in the crown, and assume a more horizontal direction in the region of the neck, while in the

* Extracted from the author's essay, "The Distribution of Living Matter in Human Dentine, Cement, and Enamel." *The Dental Cosmos*, Philadelphia, 1878 and 1879.

root they remain horizontal or sometimes turn downward to a varying extent. Besides the main sigmoidal curvature, each individual canaliculus exhibits a more or less wavy course in its way through the dentine, and the individual curvatures are, as a rule, very marked on the outer periphery of the dentine.

The dentinal canaliculi reach the outer surface of the dentine only on the circumference, which is covered by enamel, while on the periphery coated by cementum, including also the neck, the canaliculi terminate before reaching the cementum, and are replaced by a fine, granular basis-substance greatly varying in its width. The distribution of the dentinal canaliculi is in the great majority of teeth uniform throughout the dentine, although exceptionally I have met with specimens of dentine in which there were smaller or larger territories devoid of dentinal canaliculi, which latter look as if arranged in bundles or groups within the basis-substance.

Each canaliculus contains a dentinal fiber. Longitudinal sections of dentine, stained with carmine or chloride of gold, if examined with high powers — from 1000 to 1500 diameters (immersion lenses) — exhibit the following: The canaliculi of the dentine run in a more or less wavy course through the basis-substance, and are, as a rule, bifurcated only on the periphery of the dentine, both toward enamel and cementum. Each canaliculus contains a central, slightly beaded fiber, which on its whole periphery sends delicate, thorn-like elongations through the light space between the central fiber and the wall of the canaliculus. The thorns are distinctly conical, their bases being attached to the dentinal fibers, and their points directed toward the basis-substance. The smallest thorns spring in an almost vertical direction from the dentinal fiber, while somewhat larger offshoots may run obliquely through the basis-substance, and directly unite neighboring fibers with each other in the vicinity of the enamel and cementum.

The basis-substance shows a distinct net-like structure. The light spaces surrounding the dentinal fibers send delicate elongations into the basis-substance, in which, through repeated branching, a light net-work is established, the meshes of which contain the decalcified, glue-yielding basis-substance. The finest offshoots of the dentinal fibers can be traced only into the mouths of the elongations of the canaliculi; on the periphery of the latter, owing to their great delicacy, the offshoots are lost to sight. Coarser offshoots of the dentinal fibers, at the localities mentioned before, traverse the basis-substance within its light net-work, at the same time uniting dentinal fibers directly, and sending slender conical offshoots into the light net-work of the basis-substance. (See Fig. 262.)

The dentinal fibers are either in direct connection with coarser offshoots of the bioplasson bodies of the cementum, or the light net-work of the basis-substance of the dentine is in communication with that of the basis-substance of the cementum. The latter condition prevails on the periphery of the neck of the tooth, where the basis-substance of the dentine is not pierced by larger offshoots of the dentinal fibers, but only by a delicate net-work, through which the connection between dentine and cementum is indirectly established.

In cross-sections of dentine the dentinal canaliculi are visible in the shape of round or oblong holes; the center of each is occupied by the dentinal fiber, which has the shape of a small, roundish dot. Again we see that the periphery of the dentinal canaliculus is sharply marked, and repeatedly inter-

rupted, by light lines leading into the light net-work which pierces the basis-substance between the canaliculi. The central fibers look very distinct and dark violet in specimens stained with chloride of gold, and send slender, conical, radiated offshoots through the surrounding dentinal canaliculi, respectively, toward the mouth of the light interruptions in their walls. In directly transverse sections, one, two, or sometimes even three, such offshoots can be seen in a star-like arrangement. Each offshoot springs, with a broad base, from the central dentinal fiber, while its pointed end always is directed toward the perforation in the wall of the canaliculus, where, as a rule, it is lost to sight.

Toward the boundary between dentine and enamel, and dentine and cementum, as is well known, the dentinal canaliculi ramify, and according to their ramifications also the dentinal fibers bifurcate, becoming thinner the nearer to the surface of the dentine. Both longitudinal and transverse sec-

F1

F2

FIG. 262.—ROOT OF MOLAR. STAINED WITH CHLORIDE OF GOLD.

D, dentine; *C*, cement, with plastids branching and uniting; F^1, dentinal fibers, with their transverse offshoots; F^2, ramification of dentinal fibers and their union with the offshoots of cement-corpuscles. Magnified 1200 diameters.

tions of this part of the dentine show details identical with the main mass of the dentine, the only difference being that, near the periphery of the dentine, the fibers are more delicate and more closely packed together. (See Fig. 263 A and Fig. 263 B.)

In some teeth I have met, on the periphery of the dentine of the crown, with the so-called "interglobular spaces" (Czermak), which may be considered as remnants of the embryonic condition of the dentine. They represent lacunæ of greatly varying sizes, bounded by curved lines, the convexities of which are directed toward the central cavity. These spaces sometimes contain bioplasson—*i. e.*, embryonal elements which have not been transformed

into basis-substance and not calcified. The dentinal fibers enter the bioplasson bodies, and each fiber is united with the net-work of these bodies by means of delicate, thorn-like projections. At other times the basis-substance of the dentine is developed within the interglobular spaces, but devoid of lime-salts. In this instance the dentinal fibers, without investment and without changing their course, pierce the basis-substance and send offshoots to this through the surrounding light spaces.

The dentine shows peculiar formations in general, though not constantly, as instanced when approaching the enamel and cementum. These formations, however, being in close relation to the covering tissues of the tooth, I prefer to describe in the chapter on cementum and enamel.

Cementum. It has been long known that there exists a striking analogy between the structures of the cementum and bone.

If we consider the central or pulp canal of the tooth as a formation analogous to a Haversian canal, containing blood-vessels, nerves, and medullary tissue, then the surrounding cementum corresponds to a Haversian system of ordinary bone, between which and the pulp-canal there exists an intermediate stratum of dentine.

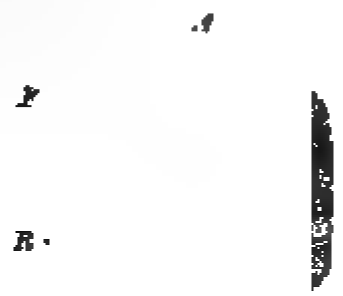


FIG. 263 A.—CROSS-SECTION OF DENTINE OF INCISOR. STAINED WITH CHLORIDE OF GOLD. MAIN MASS OF DENTINE.

F, dentinal canaliculi with the central dentinal fiber, the latter with star-like offshoots. *R*, the basis-substance between the canaliculi, pierced by a delicate light network. Magnified 2000 diameters.

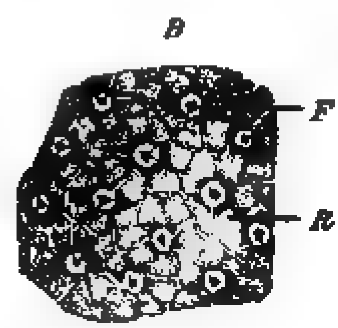


FIG. 263 B.—CROSS-SECTION OF DENTINE OF INCISOR. STAINED WITH CHLORIDE OF GOLD. VIEW FROM OUTER PERIPHERY OF DENTINE, NEAR ENAMEL.

F, dentinal canaliculi with the central dentinal fibers, the latter with star-like offshoots. *R*, the basis-substance between the canaliculi, pierced by a delicate, light network. Magnified 2000 diameters.

The zone of dentine is not present all around the pulp-cavity on the apices of the roots; there the cementum, being the outermost layer of the tooth, directly lines the cavity.

Delicate parallel striations are to be seen in the cementum, identical with the lamellæ of a Haversian system, and, as a rule, more plainly marked near the periphery than toward the dentine.

Within the basis-substance of the cementum there are numerous branching spaces, in correspondence with the lacunæ of bone. The offshoots of these spaces in the cementum, like the spaces themselves, are very marked in dry specimens, because of their being filled with air. In chromic acid specimens, on the contrary, the offshoots are much less prominent, and the less the more thoroughly the decalcification has been effected by the acid. No essential difference is noticeable between the lacunæ and canaliculi of ordinary bone and those of the cementum; in both tissues there exists a great variety as to

the general arrangement, the size of the lacunæ, and the number and ramifications of their offshoots.

The walls of the lacunæ and the coarser offshoots, if viewed with a highly magnifying lens, appear interrupted at their peripheries by light spaces, which lead into a light, delicate net-work, piercing the whole basis-substance to such an extent that only the meshes have to be considered as the fields of calcified glue-yielding basis-substance. Each lacuna contains a plastid with a central nucleus—the cement-corpuscle. The nucleus sometimes is relatively large and surrounded only by a narrow seam of bioplasson; while in some small lacunæ a body of the appearance of a nucleus is present without a noticeable amount of surrounding bioplasson. The net-like structure of the plastids is plainly visible on all cement-corpuscles. From their periphery conical offshoots arise, the coarser of which penetrate into the larger offshoots of the lacunæ, while the finest offshoots traverse the light rim between the wall of the lacuna and the periphery of the plastid, being directed toward a light interruption on the boundary of the lacuna.

Cement-corpuscles, on the average, are round or spindle-shaped bodies, the long diameter of which corresponds to the direction of the lamellæ. In teeth of juvenile and middle-aged persons we meet with cement-corpuscles surpassing three or four times the size of ordinary ones, in which two or three nuclei are visible. Instead of multinuclear bodies, a number of medullary nucleated elements may fill a large lacuna. Numerous cement-corpuscles send broad and branching offshoots through the basis-substance in a vertical or oblique direction to the lamellæ, and not infrequently a direct union is established between two or three cement-corpuscles by means of such large offshoots (see Fig. 262).

In some teeth, broad, spindle-shaped spaces pierce the cementum in a radiated direction, all of which contain bioplasson with delicate offshoots directed toward the net-work in the basis-substance. Nay, sometimes medullary spaces traverse the lamellæ in different directions, which, besides a varying number of medullary elements, contain capillary blood-vessels, evidently in connection with the capillaries of the pericementum. These formations may be considered as remnants of the embryonic condition of the cementum, and are never present in large numbers. All plastids within the cementum, though greatly varying in shape, agree in being connected with each other by the delicate net-work which pierces the basis-substance.

At the periphery of the cementum, on the line of the connection with the pericementum, the net-work of the bioplasson is usually very broad, and the fields of the basis-substance show a prevailing globular appearance. Also, numerous spindle-shaped plastids are seen in connection with the cementum in an oblique arrangement, forming the transition into the structure of the pericementum. Between the calcified cementum and the striated connective tissue of the pericementum there often exists a narrow zone, occupied by closely packed spindle-shaped bodies only.

The connection between dentine and cementum is established either by a gradual change of one tissue into the other, without a distinct line of demarcation, or there exists a boundary formed by a more or less marked wavy line, presenting irregular, bay-like excavations. Lastly, it occurs that between the bay-like excavations and the dentine there is interposed a stratum of the structure of cementum, with a gradual change of the tissue of the former into that of the latter.

Where a gradual change takes place, the dentinal canaliculi show irregular, mainly spindle-shaped, enlargements, which stand in the direction of the dentinal canaliculi themselves, or run obliquely through the basis-substance of the cementum. The distal end of such a spindle is, as a rule, in connection with a regular lacuna of the cementum, or with an analogous formation of a neighboring dental canaliculus. Many of the latter simply pass into the light, delicate net-work characteristic of the basis-substance of cementum. The dentinal fiber is in direct union with the bioplasson, which fills the spindle-shaped spaces, or it is lost to sight upon entering the net-work of the basis-substance of the cementum. (See Fig. 264.)

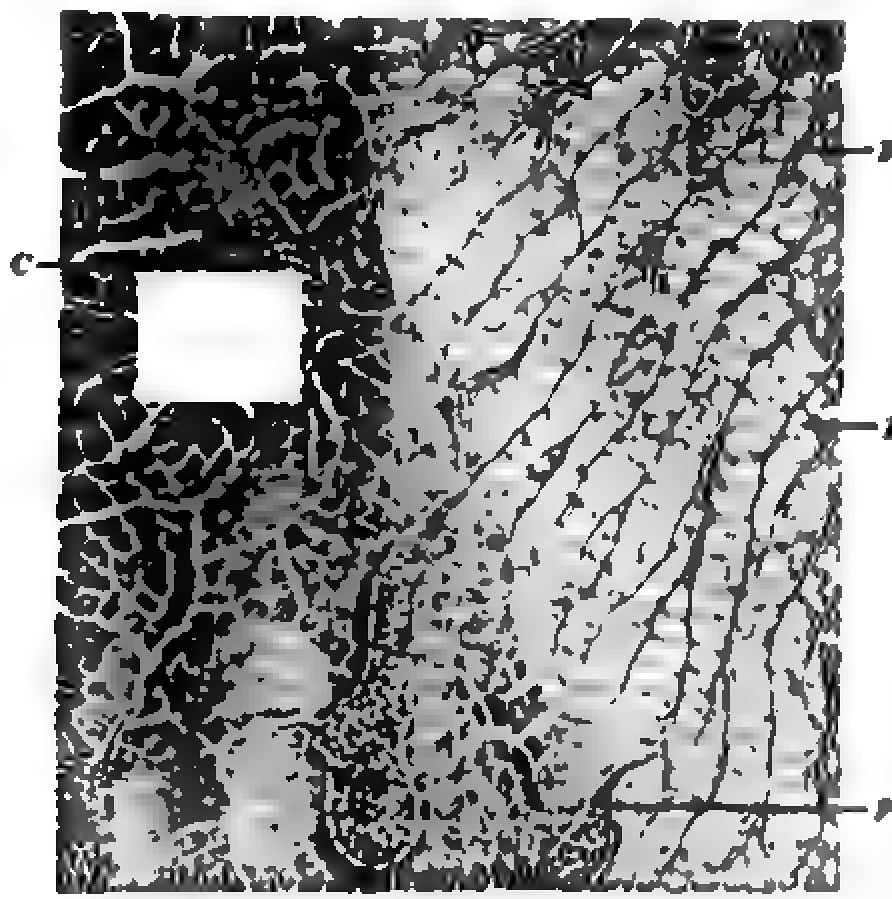


FIG. 264.—TRANSITION OF DENTINE INTO CEMENTUM, WITHOUT A MARKED BOUNDARY.

C, branching cement-corpuscle; P, spindle-shaped cement-corpuscle, both in direct connection with dentinal fibers, F, which bifurcate within the canaliculi of the dentine, D. Magnified 1200 diameters.

Where a boundary with bay-like excavations is present between dentine and cementum, spindle-shaped enlargements of the dentinal canaliculi may be seen, much smaller than in the former instance. The majority of the dentinal canaliculi, however, reach the boundary of the cementum after repeated bifurcations, by which both the calibers of the canaliculi and their central fibers are gradually diminished in size. A connection of the dentinal fibers with the coarser offshoots of the cement-corpuscles is often observed. The light net-work of the basis-substance of the dentine always passes into that of the cementum. Not very rarely, also, on the bottom of a bay-like excavation partly nucleated plastids are present, into which the dentinal fibers inosculate. The connection between these and the coarser offshoots of the cement-cor-

puscles under these circumstances is established by such intervening bodies. (See Fig. 265.)

For the designation of the bioplasson formations between the dentine and enamel, and dentine and cementum, I adopt the term "interzonal layer," as first proposed by Dr. W. H. Atkinson.

Neck of Tooth. There are certain peculiarities about the minute anatomy of the neck of the human tooth, which, so far as I can judge from the literature within my reach, have not been heretofore mentioned.

John Tomes, in describing the distribution of the dentinal tubes, says: "Near the neck they stop short of the cementum." This assertion is in accordance with my own observations. In the great majority of teeth neither the canaliculi nor their contents, the dentinal fibers, reach

FIG. 265.—TRANSITION OF DENTINE INTO CEMENT, WITH AN INTERMEDIATE LAYER OF CEMENT-STRUCTURE.

D, dentine; *F*, bifurcating dentine-fibers, in union with elongated cement-corpuscles, C^1; these are imbedded in a basis-substance blending with that of dentine. The regular cementum is characterized by branching corpuscles, C^2. Magnified 1200 diameters.

that part of the cementum which surrounds the neck. Near the periphery of the dentine bifurcations of the canaliculi—and consequently also of their tenants, the dentinal fibers—take place, some of the finest terminations of which run to the boundary between the dentine and cementum. As a rule, the finest terminations of these fibers are lost to sight in a net-work somewhat coarser than that of the basis-substance of ordinary dentine. Sometimes the

dentinal canaliculi, when approaching the periphery, become slightly dilated, so as to produce slender, pear-shaped cavities, in accordance with which the terminating dentinal fibers exhibit slight enlargements.

The boundary between dentine and cementum presents a wavy line, traversed by delicate threads, or occupied by spindle-shaped bioplasson formations, all of which are in union with direct or indirect elongations of the dentinal fibers.

The cementum around the neck forms a narrow layer, which is cut off obliquely at the place of junction with the enamel. Both the cementum and enamel in this situation—being of the same width—are separated by a boundary which runs from the outer periphery obliquely downward to the dentine. This relation I found in the majority of teeth, and it is only exceptionally that I have met with cementum overlapping the enamel. The cementum on the neck is built up by delicate prisms, or spindles, arranged

D

DI

Cc

N

DP

Fig. 266.—Anomalous Formation of Cementum on the Neck of a Human Tooth.

D, dentine; *N*, cementum on neck of tooth, with spindle-shaped or prismatic fields of basis-substance; *DP*, depression in the cementum of the neck, filled with elements of pericementum, *P*, surrounded upward by a zone of regularly developed cementum, *Cc*. Magnified 1200 diameters.

vertically to the surface of the dentine. The prisms represent the fields of the basis-substance, and are separated from each other by light rims, holding beaded fibers, or traversed by delicate vertical threads. In transverse sections, when the prisms are cut obliquely, they exhibit irregular, opaque fields, separated from each other by light rims.

The cementum on the neck of the tooth is devoid of lamellæ and lacunæ, which appear deeper below, together with all the characteristic features of the fully developed structure of the cementum. The lamellæ become the

more distinct, and the lacunæ, with their contents (the cement-corpuscles), the more numerous, the broader the diameter of the layer of the cementum.

The outer surface of the cementum is covered on its upper part with a narrow layer of connective tissue and with epithelial elements, in close resemblance with those of Nasmyth's layer of the enamel. This layer turns over into the epithelial coat of the gum.

I have met once with striking formations on the neck of a tooth. The ordinary cement of the neck is interrupted by grooves or pits containing the elements of pericementum. The inner periphery of the pit is covered with a well-developed, evidently isolated, formation of cementum. The island of the cementum is broadest above the bottom of the pit, and slopes down along the walls of the pit until it is lost within the layer of the cementum of the neck. (See Fig. 266.)

FIG. 267.—LONGITUDINAL SECTION OF ENAMEL.

ER, enamel-rods, traversed by prevailing vertical spaces; *EF*, enamel-fibers, branching and partly uniting by delicate offshoots. Magnified 1200 diameters.

Enamel. Up to this time the impression of most examiners has been that the enamel is built up by bundles of rods or prisms, crossing each other, and traversed by faint vertical lines, which give each of them the appearance of a column subdivided into small squares. The enamel-rods doubtless exist, and are wavy close to the dentine, and straight on the periphery and the main mass of the enamel. They may be considered as columns of a calcified substance, between which minute spaces are left, analogous to the cement-substance of epithelial formations.

In longitudinal sections we see delicate beaded fibers, which occupy the central portion of the interstices between the enamel-rods. These fibers I propose to term the "enamel-fibers." From such a fiber arise very minute conical fibrillæ, which traverse the rims between the fiber and the neighboring outlines of the rods, and fade away from the moment they enter the latter. The columns of the basis-substance themselves are pierced by delicate canaliculi, running in an almost vertical direction through the enamel-rods, regularly enough to give the appearance of squares, although these are much smaller than usually represented. In the middle of a minute square light canals are seen, not infrequently running parallel with the outlines of the enamel-rod. The square fields thus produced by the rectangular crossing of light channels look, under the power of 1200 diameters, finely granular. In specimens not fully decalcified it is impossible to decide whether there is a light net-work within the enamel prisms analogous to that in the basis-substance of the dentine and cementum, or whether the granular appearance is merely due to the depositions of lime-salts. (See Fig. 267.)

Cross-sections of the enamel, which we obtain also in longitudinal sections of the tooth, on account of the different directions of the bundles of the enamel-rods, plainly exhibit the irregular polyhedral fields of the enamel-rods. The light interstices between the polyhedral fields contain in many instances delicate beaded fibers surrounding the polyhedral fields of the enamel-rods. The fibers, if cut transversely, have the appearance of dots, and connect with each other directly or by means of intervening delicate

threads. Extremely fine thorns traverse in a vertical direction the light space between two neighboring enamel-rods, even where a fiber is not visible. (See Fig. 268.)

The rods of the enamel, on an average, are half the diameter of the columns of the basis-substance in dentine; therefore four columns of the former will correspond to two of the latter. Sometimes in the cross-section of an enamel-rod I met with roundish formations occupying the center of the rod, one or two in number, which, owing to a denser granulation and a surrounding shell, have the appearance of nuclei. The enamel-fibers run a very straight course toward the surface, and are here usually a trifle thicker than near the boundary of the dentine.

The outermost surface of the enamel is covered by flat epithelia (Nasmyth's membrane), which, in the transverse section, have the appearance of flat spindles; not infrequently there also occurs a stratified epithelium on the surface of the tooth. The enamel-fibers are in connection with these epithelial bodies, which, if detached, show delicate offshoots adhering at regular intervals—the broken enamel-fibers. Sometimes the surface of the enamel is coated by a thin, uniform layer, with regularly scattered nuclei.

ER

EF

FIG. 268.—CROSS-SECTION OF ENAMEL.

ER, rods of enamel, partly exhibiting formations like nuclei, the light interstices between the rods traversed by delicate beaded fibers, *EF*, or by vertical thorns. Magnified 2000 diameters.

At the place of junction of the enamel with the dentine a direct connection is often seen between the enamel and dentine fibers. The latter, through repeated bifurcations, being closely brought together, continue their course into the enamel-fibers without any interruption. The direction of the fibers of the two tissues, however, is almost never identical, inasmuch as the enamel-rods, and consequently the enamel-fibers, as a rule, owing to their wavy course in this situation, are obliquely intercepted upon the dentine.

We can very often trace dentinal fibers up into the enamel in a varying distance, without a distinct union between the enamel and dentine-fibers, as the former do not reach the surface of the dentine, but terminate above its level at different heights, while the zone close above this is occupied by a delicate, irregular net-work analogous to that of the dentine. (See Fig 269.)

In many places the dentinal canaliculi upon entering the enamel suddenly become enlarged, and form more or less distinctly spindle-shaped cavities of greatly varying diameters, analogous to the spindle-shaped enlargements at the boundary of the cementum. These enlargements run either in the main direction of the dentinal canaliculi or deviate obliquely. They invariably contain bioplasson bodies, which plainly show the reticular structure, and sometimes contain one or more compact clusters to be considered as nuclei. The spindle-shaped bodies, on their proximate ends, are in direct connection with the terminations of the dentinal fibers which have arisen from their repeated bifurcations, while on the distal end they may show delicate fibers—viz.: enamel-fibers—or delicate conical thorns traversing the light space between the surface of the bioplasson body and the wall of the cavity. These thorns are lost to sight on passing into the net-work at the bottom of the enamel.

In some places, especially on the cusps, the spindle-shaped enlargements of the dentine-fibers are quite numerous, and of an almost uniform size and direction, forming regular rows of spindles within the enamel. In the teeth of younger individuals the spindle-shaped enlargements are comparatively larger and more regular than in the teeth of old people.

The boundary line between the dentine and enamel is either straight or slightly wavy, and with more or less deep, bay-like excavations, analogous to those on the boundary between dentine and cementum. The concavities of the bays are directed toward the dentine. In this interzonal layer at the bottom of the bays we meet with fibers occupying the curved spaces between dentine and enamel, or we see, in a correspondingly bent direction, bioplasson bodies directly connected with the dentinal fibers downward, and with the enamel fibers upward. (See Fig. 270.) In specimens stained with chloride of

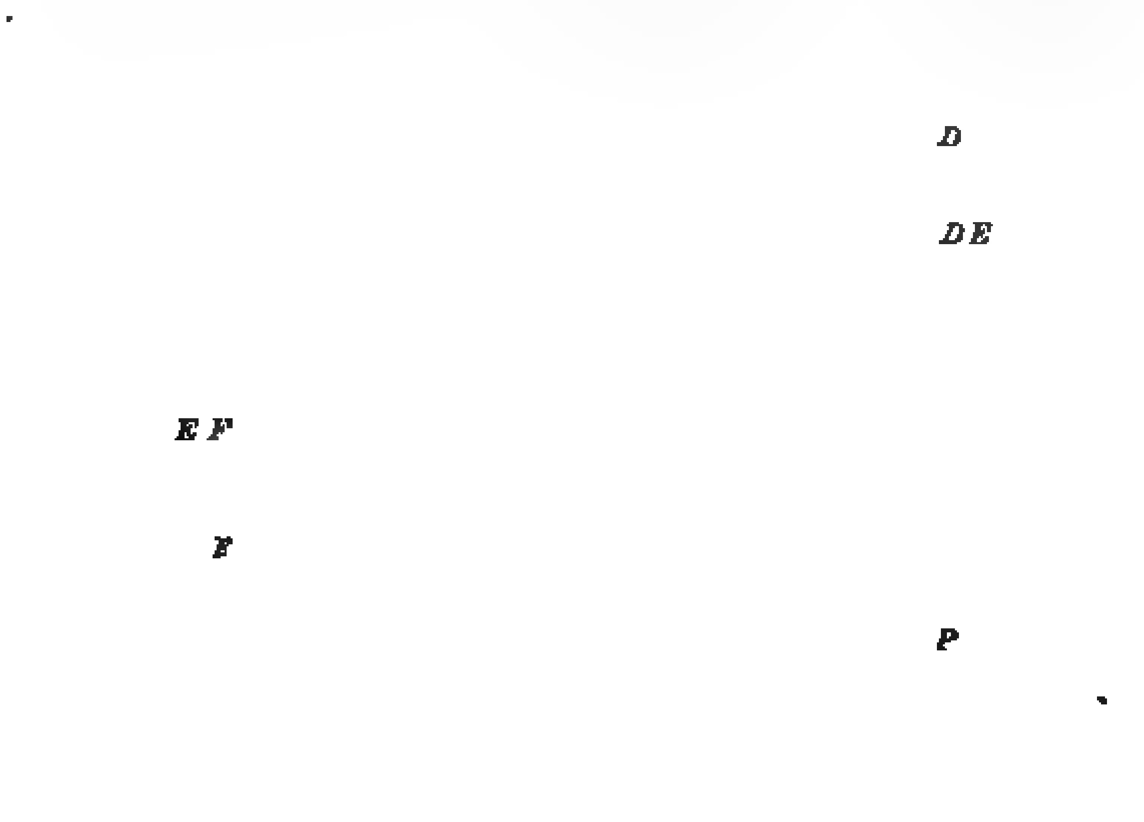


FIG. 269.—UNION OF DENTINE WITH ENAMEL.

D, dentine; *E*, enamel; *DF*, dentinal fibers, being in union with large bioplasson bodies, *P*, or directly running into enamel-fibers, *EF*; the latter often are lost in the delicate, irregular net-work on the bottom of the enamel. Magnified 1200 diameters.

gold the dentine is always much deeper in color than the enamel, hence the relations described are very plainly marked on such specimens.

Results. The details described make it evident that we shall have to modify considerably the views heretofore maintained on the structure of the teeth. Since we have known the structure of "protoplasm," and that of basis-substance of connective tissue, by the researches of C. Heitzmann, we are accustomed to look for the distribution of the living matter not only in the plastids (the formerly so-called cells), but also in the basis-substance, which formerly was thought to be devoid of life.

The structure of the tooth closely resembles that of bone. We know that the basis-substance of bone is traversed everywhere by a net-work of living

matter, in the shape of beaded fibers, where they form larger offshoots of the plastids. Similar features are also present in the tissues of the tooth.

(1) *The dentinal canaliculi are excavations in the basis-substance of the dentine, each containing in its center a fiber of living matter. Besides the dentinal canaliculi, there exists an extremely delicate net-work within the basis-substance of the dentine, into which innumerable offshoots of the dentinal fibers pass. Although we cannot trace the living matter throughout the whole net-work in the basis-substance, we are justified in assuming that not only the dentinal canaliculi, but the whole basis-substance of the dentine, is also pierced by a delicate net-work of living matter. The living matter of the dentine is in direct union with that of the bioplasson bodies of the pulp, of the cementum, and of the enamel.*

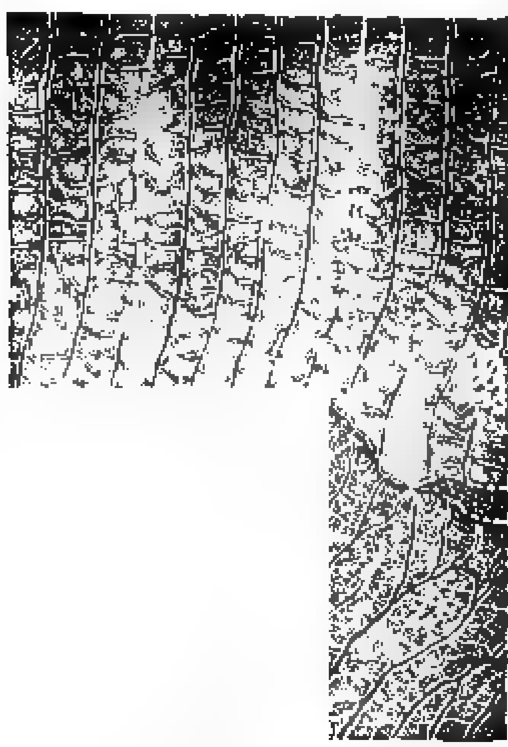


FIG. 270.—UNION OF DENTINE WITH ENAMEL.

D, dentine; *E*, enamel, *P*, bioplasson formations at the boundary between both tissues, in union with enamel-fibers, *EF*, and with dentine-fibers, *DF*. Magnified 1200 diameters.

(2) *The cementum, as well as ordinary bone, is provided with lacunæ and canaliculi. The lacunæ contain nucleated plastids, and the canaliculi hold offshoots of the living matter of the plastids. The whole basis-substance of the cementum is traversed by a delicate net-work, which in all probability contains living matter, though this is traceable only in its thorn-like projections from the periphery of the plastids and their larger offshoots. The living matter of the cementum is uninterruptedly connected with that of the pericementum, and continuous with the living matter of the dentine, either through intervening bioplasson bodies in the interzonal layer, or directly with the dentinal fibers.*

(3) *The cementum covering the neck of the tooth is devoid of lamellæ and plastids. It is built up by directly ossified osteoblasts of the pericementum, presenting their prismatic shapes, and everywhere traversed by a net-work of living matter. This is in connection with the pericementum, and with the dentine mainly through the intervening net-work in the basis-substance of the latter.*

(4) *The enamel is traversed by fibers of living matter located in the interstices between the enamel-rods. The fibers are connected with each other by delicate fibrillæ, piercing the enamel-rods in a vertical direction. The enamel-fibers send conical thorns toward the enamel-rods, and such thorns are visible in all interstices between the enamel-rods. The enamel fibers are continuous on the outer surface with the covering layer of flat epithelia, and on the inner surface with the dentinal fibers. The latter connection is either direct or indirect through a net-work of living matter, or through intervening bioplasson bodies in the interzonal layer.*

History. It is not my intention to traverse the entire history of microscopical studies regarding the structure of teeth. I propose to quote only

from representative writers on odontology, in order to show how the present theories on this subject have been gradually developed.

I quote from John Hunter *: "Enamel has no marks of being vascular, and of having a circulation of fluids; it takes no tinge from feeding with madder, even in the youngest animals. This looks as if the enamel were the earth more fully depurated, or strained off from the common juices in such a manner as not to allow the gross particles of madder to pass. The other substance of which a tooth is composed is bony, but much harder than the most compact part of bones in general."

Joseph Fox † says: "The enamel, when broken, appears to be composed of a great number of small fibers, all of which are so arranged as to pass in a direction from the center to the circumference of the tooth, or to form a sort of radii round the body of the tooth. This is the crystallized form it acquires some time after its deposit. The structure of the teeth is similar to that of any other bone, and differs only in having a covering, which is called enamel, for the exposed surface, and in the bony part being more dense."

Thomas Bell ‡ maintains: "There are two distinct substances which enter into the composition of the teeth, essentially differing from each other in structure as well as in chemical composition; the one being organized, the other crystalline. The first, of which the mass of the tooth consists, is true bone; the second, from its appearance, is called enamel."

Alexander Nasmyth § on *cementum* says: "The cortical substance is always found on the peripheral part of the tooth, forming a layer of investment around it, and lying in close apposition with the enamel or ivory. The cortical substance has no organic connection with the enamel or ivory against which it lies, and, being softer than both, is easily detached by means of a knife. In its intimate structure it presents the characteristic corpuscles and canals of bone, the latter being filled with ossific matter, but otherwise resembling Haversian canals. In structure, *enamel* is composed of cells which are arranged in regular rows, forming composite fibers placed at nearly right angles to the surface of the ivory, the original nuclei of the cells not being persistent. *Dentine.* It has long been known that the teeth are composed of two essential chemical constituents, namely, earthy salts and animal matter. From Dr. Thomson's analysis it appears that the quantity of animal matter is very considerable, and it is evident that it is contained chiefly in the fibers, or, as they have been termed, the tubes of the ivory. It was quite evident to me, from the examination of preparations, that the so-called tube was in reality a solid fiber, composed of a series of little masses succeeding each other in a linear direction, like so many beads collected on a string."

Richard Owen, ‖ in describing the structure of *dentine*, says: "The compartments of the basal substance, which I have called 'calcigerous,' or 'dentinal cells,' and which contain the hardening salts in their densest state, are sub-circular or sub-hexagonal. The calcigerous and nutrient tubes, varying from 1-10,000th to 1-20,000th of an inch in diameter, are placed with intervals equal to from two to six of their own diameters. They are nearly parallel to one another, both in their general course and curvatures,

* "The Natural History of the Human Teeth," etc., 1778.

† "The Natural History and Diseases of the Human Teeth," 1814.

‡ "Anatomy, Physiology, and Diseases of the Teeth," 1831.

§ "Researches on the Development, Structure, and Diseases of the Teeth," 1849.

‖ "Odontography," 1840-45 (vol. i., pp. 302, 303, and 304).

but as the outer surface of the tooth exceeds the inner one in extent, the tubes slightly diverge in their course and divide, decreasing in diameter to their peripheral extremities, and rapidly so near their terminations, where they become irregularly flexuous and often interlaced. The dichotomizing calcigerous tubes send off from their sides much more minute branches, which quickly divide and subdivide in the interspaces of the trunks and penetrate the dentinal cells. The *cement*, which, with the dentine, is present in all teeth of mammalian animals, is characterized, except where it forms an extremely thin layer, by the radiated calcigerous cells, usually arranged in lines or layers parallel with the surface of the cemental coat, and with each other. The *enamel* consists of more or less curved or wavy prismatic fibers, averaging about 1-4000th of an inch in diameter, and transversely striated."

John Tomes * says of *enamel*: "The organic matter said not to belong to the class of gelatinous tissues, but to be closely similar to epithelium in its chemical relations, is stated not to exist between, but in the substance of the prisms (Hoppe-Seyler). The enamel is made up of parallel fibers, which lie in close contact with one another, no intervening substance being demonstrable." On *dentine*: "In the crown of the tooth the dentinal tubes terminate by forming loops, or become too minute to be traced, or pass into the enamel and become lost. In teeth the dentine of which is imperfectly developed, the terminal branches are lost among, or end in, the minute cavities which abound in the layer at or near the peripheral surface of the dentine. Near the neck they stop short of the cementum, but toward the end of the root they not uncommonly pass into the cementum and connect themselves with the lacunæ. By the extension of the dentinal tubes into the enamel and into the cementum, a connection is formed more intimate than mere superposition and adhesion of the one to the other would have established. In preparations in which we are fortunate enough to retain a portion of the pulp with the dentine, it may readily be seen that the soft fibrils are processes of the cells known as 'odontoblasts,' which constitute the peculiar layer called the membrana eboris. It is absolutely certain that no structures other than nerves have the power of conducting sentient impressions, and hence it is not quite necessary to assume that the dentinal fibers are actual nerves before allowing them the power of communicating sensation. The greater degree of sensitiveness observable in the dentine immediately below the enamel—that is, at the point of ultimate distribution of the dentinal tubes, and consequently of their contents—may be fully accounted for on the supposition that the latter are organs of sensation, the highest sensibility of which is confined to their branches." On *cementum*: "The canaliculi of neighboring lacunæ anastomose freely with each other, and establish a net-work of communication throughout the whole body of the cementum, and occasionally become connected with the terminal branches of the dentinal tubuli. It is to the description of primary bone that the cementum of the teeth is most closely allied, and from that it is difficult to point out any distinguishing structural character."

Charles S. Tomes † maintains of *enamel*: "In perfectly healthy human enamel the fibrillar arrangement is not so very strongly marked; the fibers are solid, are in absolute contact with one another, and have no demonstrable intervening or uniting substance, or else inter-spaces would be left, which is

* "System of Dental Surgery," 1873. † "Manual of Dental Anatomy," 1876.

not found to be the case. In man, dentinal tubes may occasionally be seen to enter the enamel, passing across the boundary between the two tissues, and pursuing their course without being lost in irregular cavities." On *dentine:* "Each dentinal tube runs outward in a direction generally perpendicular to the surface toward the periphery of the dentine, which, however, it does not reach, as it becomes smaller, and breaks up into branches at a little distance beneath the surface of the dentine. The tubes have definite walls, and are not simple channels in the matrix. These walls are composed of something singularly indestructible. Indeed, the walls of the dentinal tubes are so indestructible that they may be demonstrated in fossil teeth, in teeth boiled in caustic alkalies, or in teeth which have been allowed to putrefy. Similarly indestructible tissues are, however, to be met with surrounding the Haversian canals and the lacunæ of bone. Each canal is occupied by a soft fibril, which is continuous with the odontoblast cells upon the surface of the pulp; the existence of these soft fibers was first demonstrated by my father. In the dentine, then, we have (1) a matrix permeated by tubes; (2) special walls of these tubes, or dentinal sheaths; and (3) soft fibrils contained in these tubes, or dentinal fibers. . . . Owing to their breaking up into minute branches, some of the tubes become lost as they approach the surface of the dentine, and apparently end in fine-pointed extremities. Some terminate by anastomosing with terminal branches of others, forming loops near to the surface of the dentine; others terminate far beneath the surface in a similar way. Some tubes pass into the small, interglobular spaces which constitute the 'granular layer' described by my father, while others again pass out altogether beyond the boundary of the dentine and anastomose with the canaliculi of the lacunæ of the cementum. The enamel also may be penetrated by the dentinal tubes, though this, when occurring in the human subject, must be regarded as exceptional and almost pathological in its nature. Of the real nature of the dentinal fibrils some doubts are entertained. . . . Nerves, in the ordinary sense of the word, they are not, and have never been supposed to be. . . . The *cementum*, in my opinion, is present in a rudimentary condition upon the teeth of man, etc., as Nasmyth's membrane. It consists of a calcified matrix or basal substance, to a slight extent laminated, and lacunæ. Many of the lacunæ in cementum are connected, by means of their canaliculi, with the terminations in the dentinal tubes; they, by the same means, freely intercommunicate with one another. In the fresh condition it appears probable that the lacunæ are filled up by soft matrix."

Carl Wedl* says: "Isolation of the enamel-fibers may easily be effected by means of dilute hydrochloric acid. The fibers, becoming swollen and varicose, present on the depressed portions an apparent transverse striation, and between the opposing contiguous portions narrow, fissure-like intervals remain, which have given rise to the view entertained by some investigators that canals are found in the enamel. The junction of the enamel with the dentine is effected by a transparent, irregular, wavy boundary layer, which in some parts is encroached upon by separate dentinal canals, and in others by elongated, cleft-like cavities, of irregular shapes and different dimensions. Into these cavities, which are mostly filled with opaque, amorphous, calcareous masses, one or another of the dentinal canals frequently enters. The cement has an organic connection with the periosteum of the root or root-membrane. Sometimes the canaliculi radiate from the bone-corpuscles in

* "Pathology of the Teeth," 1872.

parallel rows, and extend a considerable distance without forming a net-work. The dentine and cement are connected together by means of a layer composed of an agglomeration of transparent globules, of varying degrees of thickness. The spaces intervening between the latter (interglobular spaces) are irregularly notched, and frequently in very close proximity to one another; they are filled with an opaque, granular, calcareous substance, and very often are in direct connection on one side with dentinal canals, and on the other side with the bone-corpuscles of the cement. Sometimes this intermediate layer is very finely granular, and the spaces between the grains are exceedingly small. The cement proper commences outside of this layer, and its canaliculi rarely come into direct connection with the dentinal canals."

From W. Waldeyer * I quote : "The chief components of *dentine* are a very firm matrix, analogous to compact bony tissue, and extremely fine, frequently branched, fibers,—the dentinal fibers of Tomes and Kölliker,—which occupy fine canals, the dentinal canals traversing the matrix. The dentinal fibers are enormously elongated processes of the so-called dentinal cells, or cells of the dentinal pulp (odontoblasts). The dentinal fibers constitute the soft parts of the dentine. They do not lie in direct contact with the hard matrix, but are invested by a sheath,—the dentinal sheath of E. Neumann,—which is intimately connected with the matrix. As a general rule, each tube extends from the pulp-cavity to the enamel or cement, giving off, in its course, numerous delicate, transverse branches. By means of these transverse branches both the tubes and their contents — the dentinal fibers — anastomose with each other. In regard to the mode of peripheric termination of the dentinal tubuli, no positive conclusion can be drawn. It is not easy to decide whether the fibers are present in the finest peripheric ramifications of the tubules. A direct passage of the dentinal tubuli into the enamel does not occur." On *enamel:* "It consists of rather elongated prisms, about three to five mm. long, which are called enamel-fibers, or enamel-prisms. The dark, transverse striæ and slight varicosities, which, especially after the addition of very dilute hydrochloric acid, occur at regular distances from one another in the isolated prisms of enamel, are very remarkable. If the treatment with hydrochloric acid be continued for some time longer, the fibers split, in the direction of the clear transverse lines, into small cubic fragments of nearly equal size, three to four mm. The enamel fibers lie in close contact with each other, without any demonstrable intervening substance. The cuticula (persistent capsule of Nasmyth) forms an extremely resistent investment, not more than one-half mm. in thickness, covering the external portion of the teeth, and disappearing wholly when they are mature." On *cementum:* "The cement is a true bony structure essentially belonging to the periosteum of the alveolus, and in man and many vertebrates forms a thin investment of the fangs of the teeth. The lacunæ are for the most part large. When the cement is extremely thin, however, they may be entirely absent, and it then presents on section a perfectly homogeneous and vitreous appearance. A similarly very hard lamella, destitute of lacunæ, occurs also in the outermost portion of the thick layers of cement."

E. Magitot † says: "The dentine is bounded throughout its whole external surface by a continuous layer of dark granulations, very numerous and of various form. This granular layer, subjacent to the enamel and cement, was taken by Retzius and J. Müller for a mass of bony corpuscles, in which ter-

* Stricker's "Manual of Histology," 1872. † "Treatise on Dental Caries," 1878.

minated the canaliculos. But an attentive examination shows that, although the granulations are continuous with the terminal extremities of the canalicules, we cannot compare them to osseous corpuscles, but that they should rather be regarded as minute pits sunk in the thickness of the ivory, at its exterior limit, to aid the communications between the tubules which permeate this tissue. . . . During life the dentinal canalicules inclose a transparent, colorless fluid, containing, according to Hannover, calcareous matter in solution. . . . For a long time there has been attributed to the ivory a sensibility of its own—an opinion still held by many, even in the admitted absence of nerve-branches, and supported by the fact that the teeth vividly perceive the impressions of temperature, of acids, etc., and distinguish the physical qualities of bodies submitted to their contact, such as grains of sand and hairs. This tactile sensibility, in fact, does not belong to the ivory, and must be attributed to the extreme facility with which this substance receives the least vibrations, the slightest disturbances which are given to it by external influences, and transmits them to the pulp, whose tissue, extremely rich in nerves, fills exactly its solid shell, and thus perceives the smallest impressions communicated to it." Of the *enamel* he asserts: "The layer of enamel surrounding the crown is composed of an infinite number of rods, prismatic by reciprocal pressure, whose length is just equal to the thickness of the tissue at the corresponding point, and intimately united without the interposition of any other substance."

DENTINE AND ENAMEL OF DECIDUOUS TEETH. BY FRANK ABBOTT, M. D.*

While engaged in the study of the process of dissolution of temporary teeth, I availed myself of the method of examination of enamel as first described by Bödecker. Specimens of deciduous teeth, if prepared in this manner, exhibit, as the most striking feature, a considerably smaller amount of basis-substance than adult teeth. As a consequence, the dentinal canaliculi are much wider, and the dentinal fibers larger; thus, the possibility of seeing the minutest relations between dentinal fibers and basis-substance is greatly facilitated.

I can add nothing to what Bödecker has described in minutest details in reference to the structure of dentine. I could easily see the dentinal fibers (which, upon being stained with carmine, assume a dark red color) running through the canaliculi up to their bifurcations, close to the enamel. I could trace the lateral conical offshoots of the dentinal fibers to the point where they enter the basis-substance of the dentine. That the basis-substance holds a delicate reticulum of living matter I am perfectly satisfied, and I base my opinion upon my researches on caries of the teeth.

As to enamel, I have never seen the minute relations marked so plainly in permanent as I find them in the temporary teeth. Here the enamel-rods are narrower, and the interstices between them wider, than in permanent or adult teeth. A power of 500 diameters of the microscope is sufficient to show plainly relations visible in permanent teeth with very much higher powers only. As a striking feature in deciduous teeth, I often found a direct connection of the fibers of the dentine with those of the enamel. Thus, the width of an enamel-rod is in full correspondence with the width of the fields of basis-

* Abstract from the author's paper, "The Minute Anatomy of Dentine and Enamel." *The Dental Cosmos*, Philadelphia, 1880.

substance of the dentine, after the bifurcation of the dentinal fibers, near the boundary between dentine and enamel.

In preparing specimens, on several portions of the crown it happened that a larger portion of the enamel was ground away than was intended—so much so that only shreds of enamel in connection with the dentine were left. On one of these places delicate beaded fibers were seen isolated on their upper ends, while their lower ends could be traced into interstices between the enamel-rods, and in connection with the ends of the dentinal fibers. No doubt here the mechanical injury done to the enamel has luckily led to a tearing out of a few enamel-fibers, which accident plainly illustrates their presence.

That enamel is not a crystal, but a tissue,—alive so long as the pulp of the tooth is alive,—no one, I think, will doubt who has studied caries and seen the pigmentation of enamel and its reaction during that process.

Secondary Dentine. By C. F. W. Bödecker, D. D. S., M. D. S.*

It is generally acknowledged that the main portion of a tooth is composed of dentine, which, on the crown, is covered by enamel. The latter is thickest around the cusps, and becomes thinner the nearer to the neck. On the root the dentine is covered by cementum, which is thinnest about the neck, and thickest on the apex of the root.

Exceptionally the relations between the three hard tissues of a tooth may be found to deviate considerably from the general rule, whereby an anomalous, though not strictly pathological, formation is produced. I extracted the canine teeth from the upper jaw of a lady forty years of age, one of which I split to obtain the pulp; the other was ground thin immediately after its extraction, for the purpose of studying enamel. The results were as follows:

The crown was built up by dentine terminating in the ordinary pointed way, and surrounded by a well-developed cap of enamel. A marked brown discoloration in the usual fan-like arrangement was noticeable in the enamel, mainly in the immediate neighborhood of the dentine, but without any decay. The dentine, beginning at the neck and extending down into the root, was divided into a broad inner portion, occupying four-fifths of the root, and a narrow outer portion all around, corresponding in its thickness to that of the cementum of normal teeth. The boundary between these two layers was everywhere well defined by a scalloped line, the concavities of which look outward. In some places several such scalloped marks ran perfectly parallel, close to each other. The boundary line, however, was traversed by the dentinal canaliculi and their tenants without change of direction. The outermost portion of the dentine of the root was surrounded by cementum, not thicker than is seen on the necks of teeth of normal development. The cementum was slightly thicker on one side of the apex of the root, exhibiting there a scanty number of cement-corpuscles, which on all other portions were wanting. The boundary between dentine and cementum was sharply defined. The former bore the characteristics of dentine in the vicinity of the neck, as the canaliculi stopped short of its surface and were replaced by a coarsely granular basis-substance. (See Fig. 271.)

Nearest to the pulp-chamber there is a zone, with scanty and irregular dentinal canaliculi—formations which we are accustomed to call "secondary dentine." Next to this is a broader layer of dentine, in which the dentinal can-

* Abstract of the author's essay. *The Dental Cosmos*, Philadelphia, 1879.

aliculi run in bundles and in a slightly irregular, wavy course. Then we see a broad portion of fully developed dentine, the canaliculi of which do not reach the cementum, but beneath the latter are replaced by a coarsely granular net-work. On the outer surface appears the relatively narrow layer of cementum of a lamellated structure. Higher magnifying powers of the microscope give an insight into the minute structure of the dentine and cementum. In the layer of dentine the terminations of the dentinal fibers are seen bifurcated, and leading toward the light reticulum, in which we assume the presence of living matter. The lamellated cementum is provided with a number of curved spindles, which in their general direction correspond to the course of the dentinal fibers, while the basis-substance between the spindles appears finely granular. On that portion of the cementum of the root which is provided with cement corpuscles a distinct boundary between dentine and cementum is wanting. (See Fig. 272.) In this tooth, therefore, the cement-layer is replaced by a regularly developed layer of dentine, the former being very thin, and, with the exception of a limited portion, devoid of cement-corpuscles.

In the crown a conical portion, the blunt lower end of which binds the pulp-cavity, exhibits a structure which doubtless has all the essential properties of dentine, though in a considerably more irregular arrangement than ordinary dentine. The regular dentine terminates almost abruptly all around the cone of the irregular dentine. On the apex of the latter, large, irregularly shaped, branching spaces are visible, all of which contain partly nucleated bioplasson formations. (See Fig. 273.) The spaces, and respectively their tenants, are mainly pear-shaped, with their bases directed toward the regular dentine, with their elongations passing into the irregular dentine. From the broad bases arise numerous conical offshoots, by means of which a direct communication is established with the dentinal fibers of the regular dentine, while other offshoots inosculate with analogous formations on the apex, thus producing a coarse net-work. From the pointed

FIG. 271.—ROOT OF AN ANOMALOUS CANINE TOOTH.

D, primary dentine; *LD*, secondary dentine, composed of two zones. *P*, pulp. *C*, cementum. *PC*, pericementum. Magnified 300 diameters.

lower ends of the pear-shaped spaces wavy canaliculi originate, which freely anastomose with each other, and traverse the whole mass of the central portion of the crown in a prevailing radiate arrangement. Their number is more scanty than in the regular dentine, so much so that relatively large territories of the basis-substance are altogether devoid of canaliculi. The latter hold delicate beaded fibers of living matter, as well as the canaliculi of normal dentine, with the exception that on the average the fibers of normal dentine are finer than those of the secondary formation. Some of these fibers are provided with lateral conical offshoots, directed toward the basis-substance, which itself shows a delicate reticular structure, of essentially the same character as I have seen in regular dentine. (See Fig. 273.)

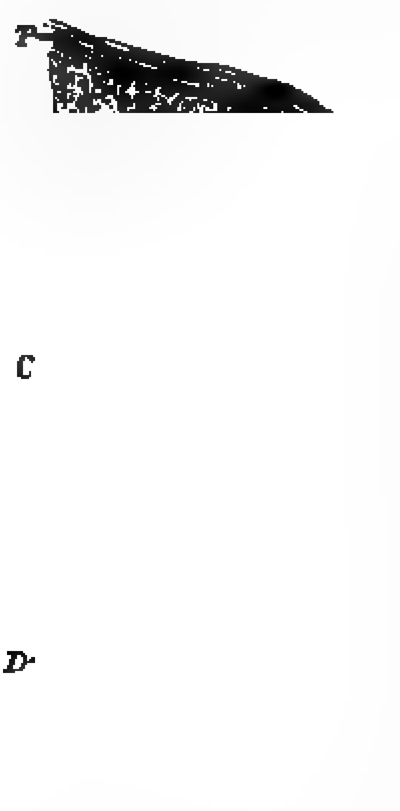


FIG. 272.—ROOT OF AN ANOMALOUS CANINE TOOTH.

D, dentine; *C*, cementum; *P*, pericementum. Magnified 1000 diameters.

The middle portion of the pulp-cavity is bounded by a narrow zone of dentine, which is possessed of canaliculi in a smaller number than the main mass of dentine. This zone, besides, is characterized by a deep carmine stain, while the regular dentine remained almost unstained. The stained portion is inserted upon the regular dentine by means of numerous shallow excavations, and its surface is irregularly jagged toward the pulp-cavity. In the apex of the root the irregular formation of dentine again is much thicker than in the middle portion, and provided with numerous roundish spaces, all of which contain plastids, and communicate with the irregular, wavy canaliculi of the boundary layer of the pulp-cavity.

In the tooth just described we have a formation which is known by the term "secondary dentine." The literature of this subject is concisely presented by Carl Wedl,* from whom I quote the following note:

"J. Hunter† says: 'In teeth which are worn away by attrition, that portion of the pulp-cavity adjacent to the abraded surface becomes filled with a new substance, which occupies the center of the abraded surface, and generally is softer than the rest of the tissue of the tooth.' Prochaska‡ treated of the same subject in his 'Observat. Anatom. de Decremento Dentium Corp. Humani.' Oudet§ gives a good description of these new formations, which he divides into two classes—the adherent and unattached. He paid no attention to their histological structure. . . . R. Owen‖ illustrates numerous new formations of osteo-dentine, but does not go very deeply into the subject. Salter ¶ treats of osteo-dentinal formations in addition to simple calcifica-

* "The Pathology of the Teeth," Philadelphia, 1872.
† "Natural History of the Teeth," 1778.
‡ Adnotat. Academ. Prag. 1780.
§ "Dictionnaire de Médecine," article "Dent," 1835.
‖ "Odontography," 1840–45.
¶ Guy's "Hospital Reports," ix.

tions of the pulp, calcareous granular deposits. He regards them as the result of a pathological process. We are indebted to J. Tomes * for their first minute anatomical description, and to F. Ulrich, † who distinguishes in them two kinds of tissues — a dentinoid, an osteoid, and a combination of the two. Wedl ‡ and Heider and Wedl § give further anatomical details, and the latter endeavor to determine the mode of development of these new formations. R. Hohl ‖ furnishes a critical treatise, based upon independent investigations, and applies to these formations the terms odontoma, osteoma, and osteo-odontoma."

John Tomes and Charles S. Tomes ¶ say as follows: "With the advance of age, the area of the pulp-cavity becomes gradually diminished by the slow

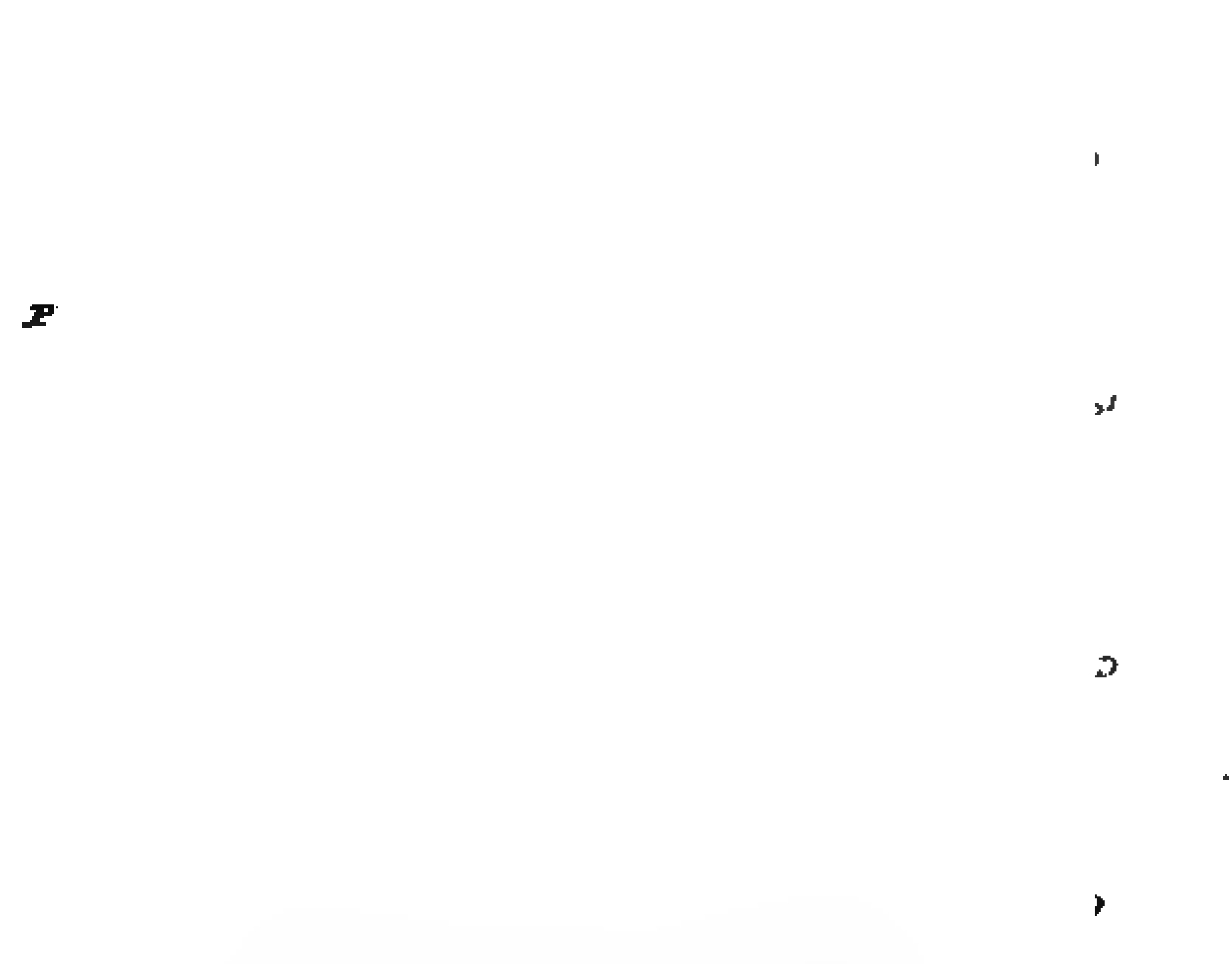


FIG. 273.—CUSP OF AN ANOMALOUS CANINE TOOTH.

D, dentine; *SD*, secondary dentine, *P*[1], pear-shaped bioplasson bodies on the boundary between primary and secondary dentine, sending large offshoots, *O*, downward; *P*[2], bioplasson body without offshoots. Magnified 500 diameters.

addition of dentine to that which was formed when the tooth was in a state of active growth; and this condition is still more strongly marked in those teeth which have been worn by mastication; indeed, in some cases the cavity

* "A Course of Lectures on Dental Physiology and Surgery," 1848.
† Zeitschrift der k. k. Gesellschaft der Aerzte zu Wien, 1851.
‡ Grundzüge der Pathol. Histologie, 1854.
§ Deutsche Vierteljahresschrift für Zahnheilkunde, 1864.
‖ "Monographie über Neubildungen der Zahnpulpe," 1868.
¶ "A System of Dental Surgery," Philadelphia, 1873, p. 307.

is almost, in others perfectly, obliterated. In either case the effect is, as respects the contraction of the cavity, general, but the local development of dentine continuous with the preëxisting tissue is very often coincident with caries. When the crown of the tooth is attacked, the pulp very commonly resumes its formative functions at a point corresponding to that toward which the disease is advancing, and adds, as it were, a patch or plate of new dentine (or secondary dentine, as it is commonly called).

S. James A. Salter * says: "Considering secondary dentine as applicable to all the after-formations of dentine by which the pulp-cavity is diminished or obliterated, I would subdivide it into dentine of repair, dentine excrescence, and osteo-dentine. I first suggested the arrangement in the 'Guy's Hospital Reports' for 1853. Osteo-dentine and dentine excrescence are not infrequently seen in teeth that are worn and exhibit dentine of repair. Dentine of repair, however, always forms upon that portion of the pulp-cavity next to the lesion, and is adherent and in direct structural continuity with the primary dentine, whereas osteo-dentine and dentine excrescence occur almost always first toward the extremity of the root, and the former is frequently quite detached from the remainder of the dentine. Mr. Salter asserts against Tomes (page 68), that 'the circumstance of age, *per se*, is really not efficient for the production of secondary dentine; and the fact that the teeth which exhibit secondary dentine are usually from aged subjects is merely accidental, and dependent upon the fact that it is in them that the teeth are most worn. Dentine excrescences are little nodules of secondary dentine, occasionally found attached to the interior of the pulp-cavities of teeth which may be otherwise healthy, unassociated with injury or other disease. Osteo-dentine is a form of secondary dentine in which the tissue combines the characters both of bone and ivory. It is usually vascular; it is frequently arranged in systems around vessels, like the Haversian systems in bone, and it sometimes contains true lacunæ."

C. Wedl *(l. c.)* accurately describes the new formations of the hard tissues of the teeth. When speaking of the new formations in the pulp-cavity, he says: "In these cases there occurs a continuous development of dentine within certain limits, determined by an irritation, and the new layers are deposited in immediate contiguity with the old, and in parts are intimately and organically united with the latter. Dentine of this description, which serves as a protective covering of the pulp, is called 'dentine of repair,'—'secondary dentine,' as is that dentine, also, which is formed in cases of chronic caries upon that portion of the wall of the pulp-cavity corresponding to the carious locality, and projects into the carious cavity in the form of a spherical segment. In the latter cases, also, we find that the new dentinal canals are continuous with the old; there is usually an abundant basis-substance, and the canals are separated by quite wide intervals. A different structure is presented by the concentrically laminated forms, two varieties of which are distinguished—the simple and complex. . . . I have met with a few cases only of true new formations of osseous substance within the parenchyma of the pulp. The greater portion of the very common osteo-dentine formations is composed of dentine; the bony substance occurs in a very small quantity, and may consist merely of a group of a few bone-corpuscles. The osseous substance not infrequently attains only a rudimentary development, and resembles that which occurs upon the cement toward the neck of the tooth."

* "Dental Pathology and Surgery," New-York, 1875.

Charles S. Tomes * says: "Secondary dentine occurs in the teeth of aged persons, in which the pulp-cavity is much contracted in size, and also is very frequently formed as a protection to the pulp, when threatened by the approach of dental caries, or by the thinning of the walls of the pulp-cavity through excessive wear." Tomes illustrates secondary dentine filling up one of the cornua of the pulp-cavity from a human molar affected by caries, which figure closely resembles the formation I have described above. Tomes remarks: "It would be impossible to attempt to give any description of the almost endless minor modifications of the dentine structure."

From the facts recorded in dental literature, it is evident that there are several causes universally agreed upon as to formations of secondary dentine. These causes are mainly: *First*, advanced age; *second*, caries of the primary dentine; and, *third*, injuries on the external surface of the tooth.

C. Heitzmann † first drew attention to the fact that in old dogs and cats a number of Haversian canals in the compact bone become obliterated. This investigator observed that the capillary blood-vessel, which represents the last remnant of the medullary tissue within the Haversian canals, is finally transformed into a solid mass, which immediately assumes the character of the bony basis-substance. The bone-corpuscles, which under these circumstances are visible in the center of a Haversian system, are as a rule larger than those scattered within the lamellæ of an earlier formation.

If we consider the pulp-cavity as a medullary space containing blood-vessels, nerves, and medullary elements, around which are arranged the layers of dentine, enamel, and cementum, we find a coincidence of the formation of bone on the one hand, and of secondary dentine on the other, in advancing age. In both instances the medullary elements are transformed into basis-substance; the nerves, probably, after having been reduced to medullary elements, also assisting in the formation of secondary dentine; and, lastly, the blood-vessels are solidified. On an average the pulp-cavity is the smaller the older the person, until at last hardly any trace of the pulp-tissue is left, and the tooth represents an almost completely solid mass.

Opposed to carious destruction of the crown I have repeatedly met with formations of secondary dentine, as described by Salter and Wedl. This occurred, however, only in those forms of caries which have been described by Frank Abbott as chronic.

As to the irritation from without, first stated by Salter to be the cause of the formation of secondary dentine, I would add chronic pericementitis, which, when limited to one root or to a portion of the root, leads to the formation of secondary dentine in the pulp-canal of the affected root. This fact strongly supports my assertion that the tooth in its normal condition is living, and irritation of the external surface may result in a new production on the corresponding inner surface of the dentine. There are instances, however, in which neither age nor an external injury accounts for the formation of secondary dentine; and such an instance is that of the tooth above described.

The coarser anatomical relations of secondary dentine in general are accurately described by C. Wedl, with whom I fully agree. In analyzing the manifold formations of this kind, I would divide them as follows:

* "Manual of Dental Anatomy," Philadelphia, 1876.

† "Ueber Rück- und Neubildung von Blutgefässen in Knorpel und Knochen." Wiener Medicinische Jahrbücher, 1872.

First. Secondary dentine resembling primary dentine.

Second. Secondary dentine with a laminated structure.

Third. Secondary dentine in form analogous to Haversian systems. This latter variety has been termed "osteo-dentine."

Secondary dentine, with the essential structure of primary dentine, is evidently the most frequent occurrence. It never has the regular arrangement of the dentinal canaliculi as seen in primary dentine, but is marked by a lighter color, owing to the larger amount of basis-substance and the relatively small number of canaliculi, which at the same time deviate more or less from the direction of the primary canaliculi. In cross-sections of such secondary dentine — especially in specimens stained with chloride of gold — we recognize in each canaliculus a central fiber, from which delicate conical offshoots emanate toward the periphery of the canaliculus. The canaliculi, which as a rule are the wider the nearer to the pulp-cavity, are pierced on their periphery by light interruptions, leading into a delicate, light reticulum throughout the whole basis-substance. (See Fig. 274.) This secondary dentine sometimes remains in an embryonal condition, exhibiting roundish fields of basis-substance, such as are visible in the dentine of a nine-months fœtus. The medullary elements, being transformed into basis-substance, represent irregular globular bodies, between which the living matter produces the formations known as dentinal fibers. The origin of these fibers will be fully understood only after thorough investigation of the development of dentine. This much is certain, that the regular fibers of secondary dentine are also beaded, and send lateral offshoots toward the basis-substance, thus indicating the presence of living matter in the latter. (See Fig. 275.)

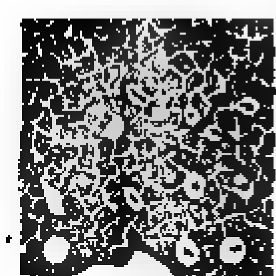


FIG. 274.—DENTINE OF AN AGED PERSON. CROSS-SECTION.

PD, primary dentine; *LD*, secondary dentine. Magnified 1000 diameters.

Formations known as "interglobular spaces" are not infrequently met with in normal dentine. They are also quite common in secondary dentine, especially on the boundary between primary and secondary dentine. The tooth first described furnishes beautiful samples of such formations. Most of these are filled with bioplasson, some exhibiting nuclei. The offshoots are evidently fibers of living matter. Some of these, toward the primary dentine, are in direct communication with its fibers; others run in different directions toward neighboring kindred formations, with which they inosculate; others, again, after repeated bifurcation, lose themselves in the basis-substance. Exceptionally there occur also bioplasson bodies without any coarser offshoots. (See Fig. 273.)

With higher amplification we see bioplasson bodies imbedded in lacunæ of the basis-substance, essentially identical with the so-called "interglobular spaces," the tenants of which never could have been made out in sections obtained from dry teeth. The plastids send larger beaded fibers in different directions into the basis-substance, which are partly in communication with fibers arising from neighboring bodies. (See Fig. 276.)

The second variety of secondary dentine consists of the formation of a lamellated basis-substance, which is traversed by irregular dentinal canaliculi.

FIG. 275.—SECONDARY DENTINE, WITH GLOBULAR FORMATIONS OF THE BASIS-SUBSTANCE.

PD, primary dentine; *SD*, secondary dentine, with irregularly scattered canaliculi; *IB*, globular bodies of secondary dentine, between which the dentinal canaliculi run, all in connection with those of the primary dentine. Magnified 500 diameters.

I have observed from my specimens that the lamellated structure begins close to the termination of the primary dentine in an almost continuous course. The lamellæ themselves never are very regular, and produce broader and narrower layers which, as a rule, are not strictly parallel to each other. In the interstices between the lamellæ, here and there, I have met with flat layers of bioplasson. The canaliculi piercing the lamellated dentine are generally very

FIG. 276.—SECONDARY DENTINE FROM CANINE.

P, bioplasson bodies with the reticular structure and offshoots, *B*, basis-substance with the light, net-like structure. Magnified 1000 diameters.

narrow, and run either in a rectangular or in an oblique direction to the lamellæ, with manifold ramifications. They invariably contain delicate beaded fibers of living matter, which send lateral conical offshoots toward the basis-substance, in a much more irregular distribution than we see in primary dentine.

Fig. 277, which illustrates the lamellated variety of secondary dentine, exhibits a peculiar feature of dentinal canaliculi in the primary dentine, near its connection with the lamellated formation,—viz.: bifurcations of the canaliculi of the primary dentine,—which otherwise do not occur except on their terminations near the enamel and the cementum.

In this group I would enumerate also those peculiar formations which have long been known by the term of "pulp-stones." The process leading to their production is by no means a mere deposition of lime-salts, but a transformation of the pulp-tissue, partly, at least, identical with lamellated dentine.

The third, and evidently rarest, form of secondary dentine is that known by the term "osteo-dentine." Formations of this kind are either peduncu-

FIG. 277.—LAMELLATED VARIETY OF SECONDARY DENTINE.

PD, primary dentine, *SD*, secondary dentine; *P*, margin toward the pulp-cavity, with bay-like excavations, due to pulpitis. The lamellæ of the secondary dentine are irregular and pierced by dentinal fibers, which are partly in direct connection with those of the primary dentine. Magnified 500 diameters.

lated—viz.: in connection with the primary dentine by a stem—or they partly fill the pulp-cavity in the shape of a uniform layer. There is a striking resemblance between osteo-dentine and Haversian systems of bone-tissue. The systems greatly vary in size and shape, and are separated from each other by a tissue kindred to primary dentine, but devoid of dentinal canaliculi. Each system has in its center a medullary canal, containing a certain amount of plastids known as medullary elements—nay, in some of the systems I have met with a central capillary blood-vessel, which has evidently been in direct union with capillaries of the pulp-tissue. Around the medullary canal a system of lamellæ is arranged, sometimes pretty regularly, and the lamellæ are traversed by delicate radiating canaliculi, closely resembling

those of bone-tissue. Only exceptionally have I seen within the lamellæ bioplasson formations analogous to bone-corpuscles. (See Fig. 278.)

In the specimen from which I have selected a spot for illustration, the lamellated systems were developed in a most marked manner; and the blood-vessels in the center of these systems were so regular that they suggested the query whether or not we had here to deal with vaso-dentine, so common in the teeth of fish. These formations occurred in the apex of the root,—some of them in the middle of regular dentine,—while the lowest systems, without any distinct boundary, were connected with the cementum, which latter, here and there, also exhibited medullary canals.

In a large number of specimens of secondary dentine I was struck by the presence of bay-like excavations on the boundary of the pulp, filled with medullary elements or multinuclear bodies (myeloid bodies or myeloplaxes). The pulp-tissue exhibited all the features of inflammation, to which also the

FIG. 278.—OSTEO-DENTINE, THE THIRD VARIETY OF SECONDARY DENTINE.

D, primary dentine, *SD*, secondary dentine; *SL*, system of lamellæ, resembling those of Haversian systems of bone; *MC*, medullary canal filled with bioplasson; *BC*, small plastids, identical with bone-corpuscles; *EP*, erosions of osteo-dentine due to pulpitis. Magnified 600 diameters.

bay-like excavations in the secondary dentine were doubtless due. If we consider the formation of secondary dentine as the result of a slight but long-continued irritation, we readily understand that such an irritation may occasionally terminate in an inflammatory process—so-called pulpitis. The newly formed dentine, partly at least, will be destroyed by the inflammation, and thus produce a combination of both formative and destructive processes, so common in inflammation of bone-tissue. The presence of inflammation would also explain the pain which sometimes accompanies the formation of secondary dentine.

THE PULP OF THE TOOTH. BY C. F. W. BOEDECKER, D. D. S., M. D. S.*

(1) *Methods.* The best method for the examination of pulp-tissue is to place the tooth, immediately after its removal from the mouth, in an aqueous solution of chromic acid, of one-half to one per cent. in strength, to which from time to time a few drops of dilute hydrochloric acid may be added. After a few weeks the peripheral portion of the dentine has become sufficiently soft to be cut by a razor. When, in cutting, the hard portions of the dentine are reached, the extraction of the lime-salts must be continued in the above described manner until the razor meets with the central cavity and its tenant, the pulp.

Another method is to split the tooth, as soon as possible after its extraction, with a strong pair of excising forceps. The teeth best adapted for this method are the incisors, canines, and bicuspids. Immediately moisten the exposed pulp with a solution of chloride of sodium, of the strength of about one-half per cent., and then remove the pulp. If the pulp is to be stained with carmine, hæmatoxylon, fuchsine, osmic acid, picro-indigo, or chloride of gold, etc., after its removal from the hard parts of the tooth, place it in the staining fluid. Among the re-agents mentioned, I have found but one of considerable value—viz.: the one-half per cent. solution of chloride of gold. This re-agent can be applied to fresh pulps as well as to very thin sections obtained after hardening in chromic acid. It may be allowed to remain in contact with the specimen for from twenty to thirty minutes. In a few days fresh specimens will assume a bright violet color, while sections which have previously been in a chromic acid solution become brownish-violet. Osmic acid, in a solution of one per cent., renders the contours of the constituent tissues, and especially those of the medullated nerve-fibers, more distinct. Both fresh and chromic acid specimens may be treated with it. Thin sections do not require more than one hour's exposure to this re-agent, while whole fresh pulps may be left in it for two or three hours. Except the ammoniacal solution of carmine, which is known to be suitable for staining certain parts of the tissue, I would not lay stress upon applying any of the other re-agents mentioned.

If a fresh pulp is thin enough it may, immediately after its removal from the split tooth, be transferred to the slide with the addition of an indifferent fluid, such as the solution of chloride of sodium. Fresh pulps of lower incisors, being the thinnest, are best adapted for examining the system of blood-vessels; shortly afterward, however, the vessels fade away. Isolated pulps may be placed between two plates of fine cork, and thus cut into thin sections with the razor.

(2) *The minute structure of normal pulp-tissue.* If we examine a thin longitudinal or transverse section of the pulp with low powers of the microscope, we recognize a large number of blood-vessels and bundles of medullated nerve-fibers. The majority of these blood-vessels are capillaries; the veins are less numerous and the arteries scarce. In many pulps we find no arteries at all, in others a limited number, particularly in the root portion of the pulp, and also in the middle of the medullated nerve-bundles. The latter mostly run in a longitudinal direction, but not infrequently we observe smaller bundles, or

* Abstract of the author's paper, "The Minute Anatomy of the Dental Pulp in its Physiological and Pathological Conditions." *The Dental Cosmos*, Philadelphia, 1882.

single medullated nerve-fibers, diverging from the longitudinal direction and running obliquely through the pulp-tissue. In transverse sections of the pulp it often happens that the nerve-fibers fall out, and then we see a roundish, empty space bounded by the sharply defined external perineurium. The absence of an endothelial coat renders such spaces easily recognizable in contradistinction to blood-vessels.

The main mass of the pulp is composed of a delicate fibrous reticulum, containing a large number of bright, shining corpuscles. Longitudinal sections in many instances exhibit delicate fibrous bundles scattered throughout the reticular structure of the pulp, mainly in the neighborhood of larger blood-

FIG. 279.—PULP OF A MOLAR. LONGITUDINAL SECTION.

M, myxomatous tissue, *V*, vein, *N*, bundle of medullated nerve-fibers; *C*, capillary blood-vessel, *B*, granular layer of basis-substance; *F*, non-medullated terminal nerve-fibers. *O*, layer of odontoblasts. Magnified 200 diameters.

vessels and nerve-bundles. Pulps composed of a fibrous connective tissue only are exceptional, and, without relation to the age of the person, very probably the result of morbid processes. Toward the outer surface of the pulp the reticular structure, as a rule, is denser than in the middle portions. This peripheral part is surrounded by a wreath of elongated formations, arranged in a radiating manner, the so-called "odontoblast layer." (See Fig. 279.)

Higher amplifications of the microscope reveal a minute reticular structure, consisting of delicate fibers, or anastomosing bioplasson cords, with very

small, oblong nuclei at their points of intersection. The meshes either look pale and finely granular throughout, or contain a bright yellowish, either homogeneous or granular, body of the size of a nucleus. The number of the latter formations greatly varies in different pulps. Where bundles of a fibrous tissue traverse the reticulum, the latter blend with the former.

In longitudinal sections the medullated nerves show the well-known fluted double contour — the sheath of Schwann. It exhibits delicate oblong or spindle-shaped nuclei. External to this we observe a delicate layer of fibrous connective tissue, the "internal perineurium." In cross-sections of the nerve-bundles more or less circular groups of medullated nerve-fibers are seen, each of which in its center exhibits the axis-cylinder in the shape of a roundish, glistening dot. Not infrequently capillary and arterial blood-vessels are met with between the nerve-fibers.

As to lymphatics of the pulp, I can say that in some specimens I have seen branches of vessels of the size of veins without an adventitial coat, being composed of large, flat, and slightly protruding endothelia.

At the periphery of the pulp the delicate reticulum constituting the pulp-tissue is very dense; here we meet with narrow capillary blood-vessels only. The outer surface of this layer is often uniformly granular, and bounded by radiating rows of shining corpuscles.

In chromic acid specimens stained with carmine, or, still better, in those treated with chloride of gold, high amplifications (1000 to 1200 diameters) reveal an extremely minute reticular structure pervading all formations of the pulp. Starting from the center of a mesh of the myxomatous tissue we see a nucleus, either homogeneous and apparently destitute of structure, or of the appearance of a vesicle with a distinct bright wall. Inside the hollow nucleus we see a varying number of bright granules interconnected with each other, as well as with the inclosing wall, by means of delicate filaments. Such filaments connect also the nucleus with the extremely delicate grayish reticulum in the light basis-substance contained in the mesh. This reticulum in the basis-substance is recognizable even though the central nucleus be absent. The fibrous or bioplasson net-work which incloses the mesh-spaces also shows a delicate reticulum in connection with the nuclei at the points of intersection.

The formations at the periphery of the dental pulp, termed *odontoblasts*, under high amplifications exhibit the following: Elongated fields, somewhat resembling epithelia, border the pulp in a radiating direction. Each field may appear in the shape of a granular bioplasson, or in that of basis-substance, in either of which oblong nuclei are imbedded in varying numbers. The nuclei exhibit coarse granules and a dense reticulum of living matter. The bioplasson bodies are separated from each other by delicate light rims, in which we see sometimes broad, sometimes delicate, transverse fibrillæ in connection with the reticulum of the neighboring formations. The bioplasson bodies or odontoblasts furnish the matrix for the basis-substance of the dentine, while the dentinal fibers, being formations of living matter, originate *between* the odontoblasts.

The medullated nerve-fibers, upon approaching the periphery of the pulp, become destitute of their myeline sheath, and, now being bare axis-cylinders, branch into numerous extremely delicate beaded fibrillæ — the "axis fibrillæ." These terminate, with knob-like extremities, in the granular layer beneath the odontoblasts, or they penetrate the light rims between the rows of the odontoblasts, and are connected with the latter by means of delicate conical

spokes. Whether the nerve-fibers directly inosculate with the dentinal fibers, I am unable to say; but I can positively maintain that an indirect connection of the two is established by the intervening reticulum of living matter. (See Fig. 280.)

The results of my researches of normal pulp are as follows:

1. *The dental pulp is a variety of connective tissue termed myxomatous, representing its embryonal form. Pulp-tissue, therefore, is a remnant of embryonal tissue, and kindred to the formations termed "adenoid tissue."*

2. *The myxomatous tissue of the pulp is intermixed with a delicate, fibrous connective tissue in varying amount. Pulps entirely, or nearly, built up by fibrous connective tissue are not to be considered physiological.*

3. *The pulp-tissue is traversed by a system of blood-vessels—viz.: arteries, veins, and capillaries. Arteries, however, are not invariably found. Lymphatics in small numbers are also present.*

4. *The pulp-tissue is richly supplied with nerves, which as bundles of medullated nerve-fibers traverse the myxomatous tissue. Toward the periphery of the pulp they become non-medullated, and terminate as minute beaded fibrillæ in knobs or between the odontoblasts.*

5. *The odontoblasts, at the periphery of the pulp, are rows of bioplasson formations, in part with nuclei*—i. e., *medullary corpuscles—such as we see wherever a new tissue arises from a former.*

6. *The dentinal fibers originate between the odontoblasts. Being formations of living matter, they are in direct connection with the reticulum of living matter; first of the odontoblasts, and afterward of the basis-substance of the dentine. The connection between ultimate nerve-fibrillæ and the dentinal fibers is very probably indirect.*

FIG. 280.—PULP OF A TEMPORARY MOLAR. STAINED WITH CHLORIDE OF GOLD.

M, myxomatous tissue; *O*, rows of medullary corpuscles so-called odontoblasts; *D*, dentine; *F*, dentinal fibers; *N*, terminal non-medullated nerve-fibers. Magnified 1200 diameters.

Pulpitis. I have examined a large number of specimens of pulpitis, but have not met with this process unless in pulp-chambers more or less reduced in their caliber by a new formation of *secondary dentine.* If pulpitis occurs at all without the previous formation of secondary dentine, this must be rare. Even where primary dentine is invaded by the inflammatory process, traces of secondary dentine are visible scattered along the pulp-chamber, and the probability is admissible that the secondary dentine has been destroyed by the inflammation to a great extent before the primary dentine was reached.

The main characteristic of this process is the appearance of a large number of inflammatory or medullary corpuscles in the pulp-tissue. These corpuscles arise from the bioplasson formations as well as from the living matter hidden

in the basis-substance. Where before a fibrous reticulum was visible containing in its meshes a basis-substance with central nuclei, in the earliest stages of inflammation numerous plastids are seen, either closely packed together in clusters or separated from each other by layers of a granular bioplasson.

The process of inflammation in many instances does not invade the whole of the pulp at the same time, but only in part.

The manner in which the inflammatory corpuscles make their appearance is as follows: Portions of living matter of either the myxomatous reticulum and its nuclei, or of the basis-substance (evidently after its liquefaction), grow into shining homogeneous lumps, from which nucleated plastids arise by a differentiation of the living matter into a reticulum. The living matter of the nerve-fibers likewise furnishes material for the formation of inflammatory corpuscles, which in slight degrees of this process are traceable in the shape of longitudinal rows. In higher degrees even these reminders of former nerve-bundles are lost. The blood-vessels soon perish on a large scale. Even in the early stages of pulpitis we have difficulty in tracing blood-vessels, as most of them are either compressed or made impermeable by a process of solidification and splitting into inflammatory corpuscles. Where blood-vessels are seen unbroken, they appear considerably dilated and engorged with blood-corpuscles. The arteries resist the destruction for the longest period of time. An artery in one of my specimens, cut transversely, shows the concentric layer of smooth muscles, divided into small lumps, and in its caliber a large number of inflammatory corpuscles, which have evidently sprung from proliferation of the endothelial coat.

As the process of pulpitis advances, at first the secondary and afterward the primary dentine is destroyed to a greater or less extent. The solid basis-substance of the dentine is at first deprived of its lime-salts, after which the gluey portion is liquefied. This process invariably takes places in the globular territories of the dentine, and by coalescence of such territories bay-like excavations originate in the dentine, at first with faint outlines, and afterward sharply defined from the calcified basis-substance. In consequence of the liquefaction, the original bioplasson condition of the dentine is reëstablished. If the inflammatory process is slow or chronic, it may happen that from a former territory of dentine, by a process of recalcification, a territory of bone is formed, in the center of which we recognize an oblong branching bone-corpuscle. This formation, however, is rathor exceptional. The rule is that the bioplasson filling a bay-like excavation becomes supplied with a number of new nuclei, thus representing the stage of a multinuclear body. Such a mass splits into a large number of inflammatory corpuscles, the sum total of which, in the bay-like excavations as well as in the pulp-tissue proper, establishes a condition termed *inflammatory infiltration.* (See Fig. 281.) In milder forms of inflammation the pulp-tissue, although considerably changed, still remains a tissue, viz., as long as the delicate filaments of living matter interconnect the single inflammatory corpuscles with one another. Should the inflammatory process abate at this stage, the tissue may proceed to the formation of a new basis-substance. Every variety of connective tissue, once inflamed, becomes a fibrous or cicatricial tissue. It is quite possible, therefore, that the few pulps I have met with exhibiting the structure of fibrous connective tissue, and scantily supplied with blood-vessels, are the products of a former inflammation. It is also probable that an advance to the formation of other tissues found in the pulp, such as dentine and bone, is the result of a slight inflammatory condi-

tion, which did not extend above the stage of hyperplasia or hypertrophy. In a few specimens of mainly fibrous structure, I have seen the bundles of medullated nerve-fibers transformed into rows of fat-globules.

Should the inflammation reach a high degree, the inflammatory corpuscles will become separated from each other,—torn apart,—and the result is the formation of pus, which, as a matter of course, is no subject of microscopical research. An intense inflammatory process very soon may lead to an engorgement of the afferent vessels and their strangulation by pressure. In this instance, death and putrefaction of the inflamed pulp will ensue.

Calcification and Waxy Degeneration. Deposition of lime-salts in the pulp-tissue is very common. It presents itself in the shape of globular, elongated, or irregular formations, of a more or less lobate surface and a high degree of refracting power. The age of the person apparently has nothing to do with

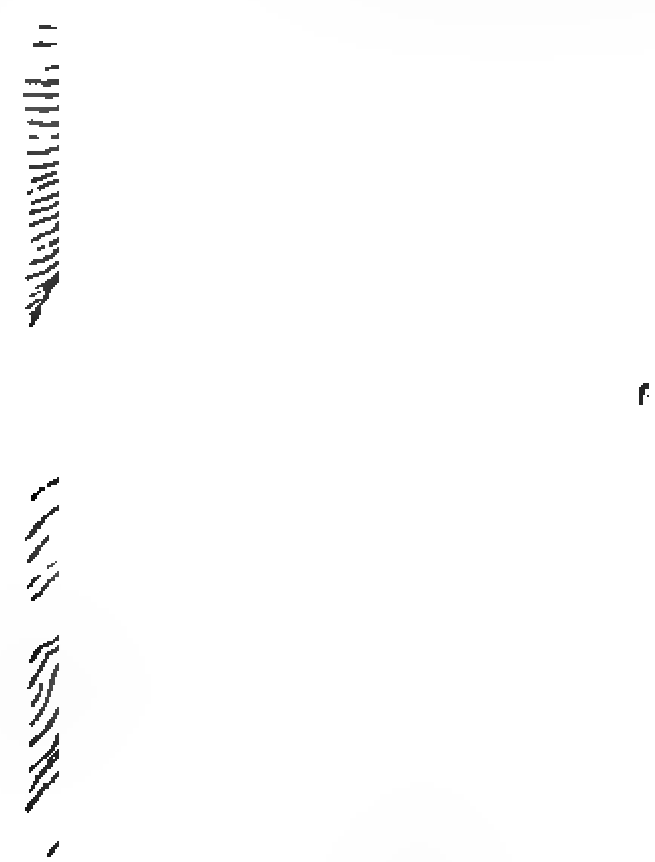


FIG. 281.—PULPITIS.

S, secondary dentine; *B*, bay-like excavations filled with medullary or inflammatory corpuscles; *M*, multinuclear body; *V*, blood-vessel in transverse section. Magnified 300 diameters.

the calcification of the pulp. I have numerous specimens of calcified pulps from apparently sound bicuspids and first and third molars of young persons, which were extracted on account of irregularity or want of room. Some of the wisdom teeth were removed when only one or two of their cusps had pierced the gums; still, their pulps exhibited calcareous depositions, as well as eburnifications.

Pulps containing a larger number of calcified spiculæ, as a rule, exhibit more fibrous connective tissue than myxomatous. Around the calcareous masses invariably a dense ensheathing layer of fibrous connective tissue has

formed. Where these masses had fallen out, an empty, fibrous sac is left behind. (See Fig. 282.) I am unable to observe any positive connection between the blood-vessels and the calcifiod masses; though sometimes a capillary blood-vessel may be attached to the capsule ensheathing the calcified mass, or it may occur that a capillary vessel is dilated like a small aneurism, and contains a calcified mass.

A peculiar change of the pulp-tissue, which I have observed both with and without calcifications, is much rarer. It consists of a transformation of the myxomatous tissue into a shining, nearly homogeneous, mass, devoid of a distinct demarcation toward the unchanged tissue of the pulp. In this homogeneous mass, which may vary greatly in extent, we recognize granular, stringy formations, and sometimes smaller bundles of nerve-fibers, not noticeably changed in their structure. In some instances, the nerve-fibers within such fields were dark and coarsely granular, as if composed of crumbs.

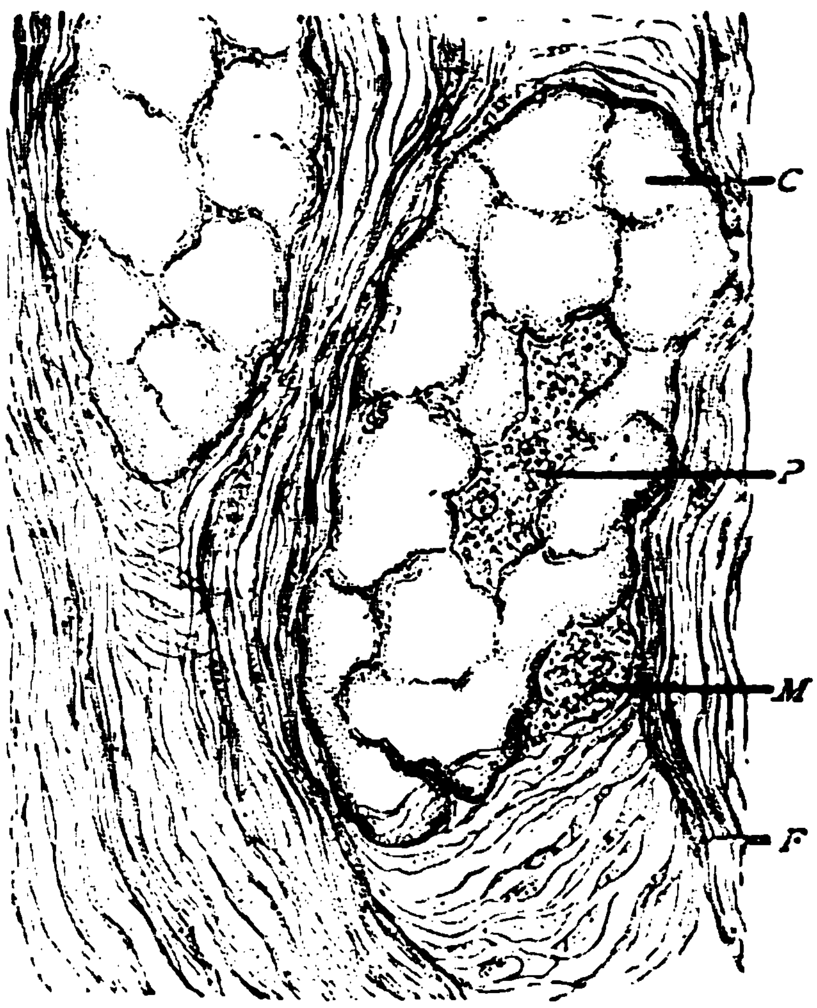


FIG. 282.—CALCIFICATION OF PULP.

C, calcareous depositions in fields corresponding to former medullary corpuscles; *M*, medullary corpuscle not infiltrated with lime-salts; *P*, plastid in the middle of the calcified mass; *F*, capsule of fibrous connective tissue. Magnified 500 diameters.

All I can say as to the re-agents applied is that the homogeneous mass stains readily with carmine.

Changes of tissues of this character are common in different organs, especially in the spleen, the liver, and the kidneys. They always indicate a low degree of nutrition, and are said to be especially caused by syphilis. This change bears the name of "*amyloid or waxy degeneration.*" Its nature, however, is far from being known.

Dentinification, Eburnification, and Ossification. It was necessary to offer new terms for the designation of a process which, although known for many years, never has been fully understood. I refer to the new formations of den-

tine in the middle of the pulp-tissue, independent of the dentine composing the walls of the pulp-chamber — the so-called "*pulp-stones.*" They, as is well known, may be found either in connection with the dentine proper, by means of a pedicle, or loosely imbedded in the connective tissue of the pulp.

Most of these formations are composed of dentinal tissue, in the form termed secondary dentine. Rarer occurrences are those exclusively constructed of a laminated bone-tissue. Somewhat rarer are combinations of both dentine and bone-tissue. The rarest are new formations of dentine strictly identical with primary dentine.

1. *Pulp-stones of the Character of Secondary Dentine.* The characteristic feature of this variety is the presence of dentinal canaliculi irregularly scattered throughout the calcified basis-substance. Sometimes the canaliculi assume a tolerably well-marked radiation; at other times, large masses of calcified basis-substance are destitute of canaliculi, which, in scanty bundles, are

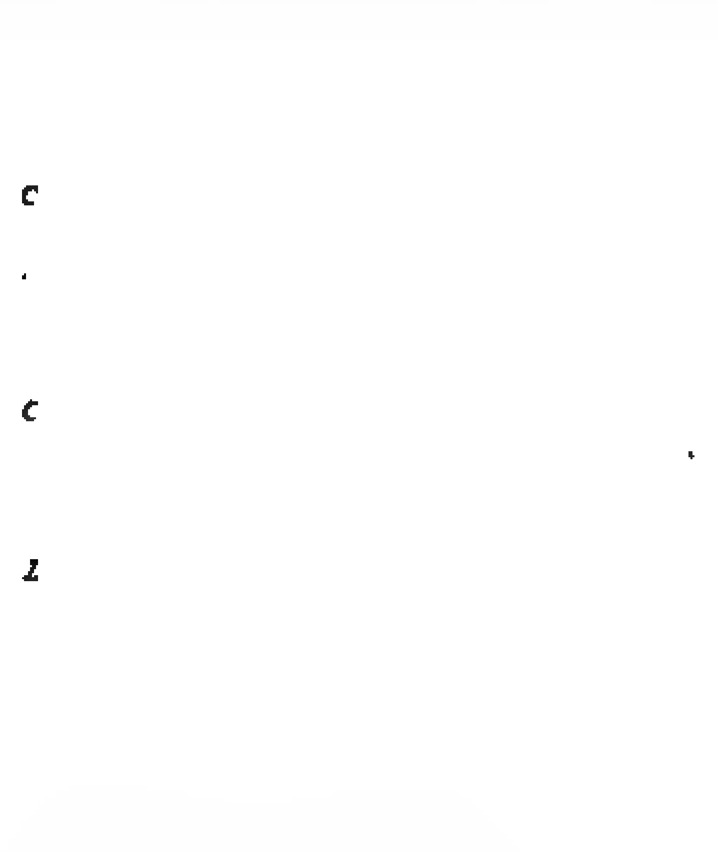


FIG. 283.— EBURNIFICATION OF THE PULP.

L, irregular lamellæ, traversed by radiating dentinal canaliculi; *CC*, concentrically striated globules (osteo-dentine). Magnified 800 diameters.

present toward the periphery of the pulp-stone. All the three varieties of secondary dentine (see page 636) may be found. Portions of the basis-substance, especially toward the periphery, may exhibit delicate concentric laminations. In the middle of an apparently homogeneous basis-substance, small, lamellated territories may occur, containing a central corpuscle with branching offshoots somewhat resembling a bone-corpuscle. In sections of one pulp-stone I have found numerous concentrically laminated territories, with either distinct or indistinct bioplasson formations in their centers. The mass between the territories was partly granular, partly composed of a tissue, like secondary dentine, with irregular canaliculi. Here and there medullary

spaces were seen traversing the tissue, from which, evidently, the new formation of the territories had started. This variety is regular osteo-dentine. (See Fig. 283.)

2. *Pulp-stones Composed of Regularly Developed Lamellated Bone.* I have observed pulps almost exclusively composed of a dense, fibrous connective tissue, the bundles of which were interlacing, so as to establish a regular cicatricial connective tissue. Scanty nerve-bundles and blood-vessels traversed this tissue, which in some places appeared to be more or less crowded with medullary or inflammatory corpuscles. In such fibrous pulps I have seen formations of fully developed bone-tissue, composed of more or less regular lamellæ, or of calcified fibrous lamellæ. In them a large number of irregular branching bone-corpuscles were seen, arranged in rows or chains, where the basis-substance was of a more fibrous character. Sometimes the bone-tissue

FIG. 284.—OSSIFICATION OF THE PULP.

L, longitudinal; *T*, transverse sections of bundles of cicatricial fibrous connective tissue. *B*, spiculæ of lamellated bone, with regularly developed bone-corpuscles. Magnified 500 diameters.

appeared in lamellated islands, sharply marked from the surrounding fibrous tissue. No formation of secondary dentine was found in these cases. (See Fig. 284.)

3. *Pulp-stones Composed of a Mixture of Regular Bone and Dentinal Tissue.* In rare instances I have met with pulp-stones composed of partly secondary dentine and lamellated bone, in such a way that irregularly bounded masses of bone contained a few large bone-corpuscles, and were surrounded by a basis-substance which held exclusively irregular, wavy, dentinal canaliculi.

4. *Pulp-stones Composed of Dentine, with the Features of Primary Dentine.* One of the pulp-stones which I examined was a mass about the size of a pea,

and built up by dentine. The canaliculi of this dentine are parallel, and between them is a finely reticular basis-substance, arranged as in the primary dentine of temporary teeth — *i. e.*, poorly supplied with lime-salts. The dentinal canaliculi are very wide; the basis-substance between them, on the contrary, is narrow. The regular dentine toward the periphery of the pulp-stone is bounded by a narrow zone, which exhibits the structure of secondary dentine. This again blends with a still narrower one composed of an indistinctly lamellated bone-tissue, with scanty but large bone-corpuscles. The bony layer is followed by the bounding layer of the specimen, of a granular appearance, containing scanty, angular or spindle-shaped bioplasson bodies and a few dentinal canaliculi. (See Fig. 285.)

C. Wedl is of opinion that these formations arise from an inversion of the odontoblasts into the middle of the pulp-tissue, believing that dentinal canaliculi can only be formed by odontoblasts. My observations demonstrate that the odontoblasts are nothing but medullary corpuscles arranged in rows. In the present stage of our knowledge we have no reason to assume that the medullary corpuscles of the periphery of the pulp are specifically destined for the formation of dentine. It is just as admissible to assume that the blood-vessels in the pulp furnish a certain variety of pabulum to the medullary corpuscles, and under the influence of this material they will be transformed into the tissue of dentine. Should medullary corpuscles, in consequence of a slight irritation or an augmented afflux of nourishing material, arise in the middle of the pulp, they may also produce dentine or bone. The laws, however, which control the new formation of tissues are as yet far from being understood.

FIG. 285.—DENTINIFICATION OF THE PULP.

PD, layer of primary dentine; *SD*, layer of secondary dentine, *O*, layer of lamellated bone-tissue; *G*, granular layer toward the pulp-tissue. Magnified 500 diameters.

History. G. Prochaska * first described that, when by attrition the teeth on their upper surfaces are worn, there is within the pulp-chamber just as much new material produced as there is worn away on the outer surface.

Rousseau † found "osteoids" and "bony growths" in the pulp-cavity, but states that Bertin has known this before him.

A. Nasmyth ‡ says: "Much diversity of opinion has already existed respecting the connection of the pulp with the ivory of the tooth, and as to

* "Oper. Minor. Anat. Physiol. et Pathol. Arg." Pars. ii., Viennae, 1780.

† "Anat. Comp. du Syst. Dent. Chez l'Homme et Chez les Princ. Animaux." Paris, 1827.

‡ "Researches on the Development, Structure, and Diseases of the Teeth." 1849.

whether the ivory be simply a product of the pulp, or a transformation of its substance." "The formative surface of the pulp displays a regular cellular arrangement. The radiating rows of cells are surrounded by a well-defined scalloped border, from which occasionally processes are observed to project at regular intervals." This author also describes and illustrates several cases of ossification of the pulp.

Kölliker * noticed new formations of dentine and cement on the walls of the pulp-cavities of teeth.

L. S. Beale † maintains as follows: "The tissue of the pulp, it must be distinctly borne in mind, is not converted into dentine; neither does dentine, nor the tissue from which it is formed, exhibit any characters which justify us classifying it with the connective tissues. I agree with Kölliker that the dentinal cells are the only active agents concerned in the formation of dentine, but cannot regard the canals as direct processes of the whole dentinal cells, nor admit that the matrix is an intercellular substance." "The mass of the pulp is composed of a simple form of connective tissue, with numerous oval and triangular corpuscles (germinal matter) not unlike that of which the mucous tissue of the umbilical cord consists."

R. J. Hulme ‡ gives a good description of the new formations in the pulp-cavity. He names four varieties, viz.: secondary dentine, dentine of repair, osteo-dentine, and nodular dentine, but he is of the opinion that the term secondary dentine would suffice for all varieties.

R. Hohl § says that new formations of dentine are found within the soft tissue of the pulp as well as on its periphery in connection with the primary dentine. The microscopical structure of these formations presents the following deviations from normal dentine: the canaliculi run in all directions; now and then they enlarge like a sac, or terminate in large holes, which, however, ought not to be regarded as bone-corpuscles. Osteo-odontomes are mixed formations, and show dentine in one and cement in another place. Osteomata are found both free and adhering to the walls of the pulp-cavity. The contents of the bone-cells, he believes, is a clear liquid, although in some places it looks granular.

Franz Boll ‖ maintains as follows: "An examination of a specimen of pulp-tissue by 500 diameters will exhibit, besides the numerous medullated nerve-fibers, a large quantity of peculiar, silk-like, shining fibrillæ, which prove to be non-medullated nerve-fibers. The transition of medullated into non-medullated nerve-fibers goes on quite gradually; the latter at first exhibit alternate expansions and constrictions in their diameters; soon they appear as naked, homogeneous axis-cylinders. The peripheral portion of the pulp is composed of a continuous layer of elongated cells, which, by long processes extending into the dentinal canaliculi, adhere to the dentine. If this film adhering to the wall of the pulp-chamber is carefully scraped off and brought under the microscope, we observe that it, besides the peripheral cells, contains some portions of the pulp-tissue. In these we notice a large number of non-medullated nerve-fibers, after teasing the specimen with fine needles. Some of these course between the peripheral cells. Although I

* "Gewebelehre," iv., Aufl. † "On the Structure and Growth of the Tissues," 1865.

‡ "On Calcification of the Dental Pulp." Transactions of the College of Dentists of England, 1861.

§ "Ueber Neubildungen der Zahnpulpe." Halle, 1868.

‖ "Archiv. f. Mikroskop. Anatomie," vol. iv., 1868.

can furnish no direct proof, I consider the prolongation of the nerve-fibers into the dentinal canaliculi as certain, the direction of the ends of the nerves being parallel with the canaliculi. In the dentine near the pulp, we have, therefore, to assume two varieties of canaliculi: those containing the processes of the peripheral cells of the pulp, and others, which receive the minute nerve-fibers emanating between these cells."

J. Bruck, Jr.,* says that the structure of dentinal new formations is identical with normal dentine, with the difference that in the former the canaliculi assume a radiating arrangement and a wavy course. Such new formations are found not only in carious, but frequently in healthy, temporary and permanent teeth. He states that all formations which previously have been described as depositions of lime-salts within the pulp are nothing else but new formations of dentine. Dentinal tissue may develop not only from the odontoblasts, but from any cell of the pulp-tissue.

John Tomes † asserts that the odontoblasts are in actual contact with one another, and there is no room between them for an intercellular substance. The most external portions of the odontoblasts undergo a metamorphosis into a gelatigenous matrix, which is the seat of calcification, while their most central portions remain soft and unaltered, as the fibrils. According to this view, the fibril, the sheath, and the matrix are but three stages in the development of the same tissue.

Carl Wedl ‡ says that the outer surface of the pulp is covered with conical cells,—the odontoblasts,—from the broad faces of which, directed outward, comparatively thick processes extend; these enter the dentinal canals. The basis-tissue of the pulp consists of a loose connective tissue. The greater portion of the very common osteo-dentinal formations is composed of dentine; the bony substance occurs in a very small amount, and may consist merely of a group of a few bone-corpuscles. With regard to the development of these isolated, encysted new formations, Heider and I have maintained the view of the occurrence of an inversion of the layer of dentinal cells. The calcareous grains are true concrements, and occur in connection with hard new formations, but never enter into organic union with the original dentine. They are located within the parenchyma of the pulp, and are calcifications in the connective tissue.

According to Waldeyer § on the odontoblasts, which are arranged so as to form a kind of columnar epithelium, three kinds of processes may be distinguished: the dentinal process, the pulp process, and the lateral processes. The first constitutes the dentinal fiber. The odontoblasts are intimately connected with each other by means of fine, short teeth, which the lateral processes of all dentinal cells form.

S. J. A. Salter ‖ says: "A very pale, ill-defined, areolar tissue, pervaded by numerous round and oval cells or nuclei, occupies the spaces between the vessels and nerves. The cellular bodies toward the surface are enlarged and assume the form of columnar epithelium. From their extremities project minute tubular prolongations, which constitute the animal basis of the dentinal tube-wall."

* "Beiträge zur Histol. und Pathol. d. Zahnpulpe," Breslau, 1871.

† "System of Dental Surgery," 1873.

‡ "The Pathology of the Teeth," Philadelphia, 1872.

§ "Manual of Histology," by S. Stricker, New-York, 1872.

‖ "Dental Pathology and Surgery," New-York, 1875.

C. S. Tomes* says: "The pulp may be described as being made up of a mucoid, gelatinous matrix, containing cells in abundance, which are especially numerous near its periphery. In it some fibrous connective tissue is discoverable. The odontoblast layer is sometimes called the membrana eboris. The odontoblasts are furnished with three sets of processes," etc., like Waldeyer. "The exact nature of the terminations of the nerve-fibers is not known."

Adolph Witzel† asserts that the odontoblasts, at their free extremities, exhibit thick prolongations, and in their finely granular protoplasm contain one or two nuclei. The new formations of dentine are composed of a finely granular or lamellated basis-substance, in which dentinal canaliculi are present, etc.

The Pericementum. By C. F. W. Bödecker, D. D. S., M. D. S.‡

(A) Forms and Development. The pericementum (root-membrane or alveolodental periosteum, etc.) is a formation of connective tissue, identical with the periosteum which covers all bones. It consists of a layer interposed between the roots of the teeth and their corresponding bony alveoli, and is common to both. It is continuous with the connective tissue — the so-called submucous layer of the gum — and with the periosteum of the maxillæ. Its fibers are connected with the cementum of the root as well as with the wall of the alveolus. A few writers have described the pericementum as a double membrane, one of which belongs to the root, the other to the alveolus; but I have not been able to see anything that justifies such a separation. Only in a few specimens have I seen, close around the root, a thin layer of very dense and fine fibers, the general direction of which was not fully identical with that of the connective tissue which produces the main mass of the pericementum.

The course taken by the connective-tissue bundles is slightly wavy and oblique, starting from the cementum and running upward toward the alveolus. The bundles of this tissue are very dense, without many decussations. The parallel direction of the bundles begins to change into a diverging one at about the height of the border of the socket, where the bundles become coarser, decussate, and thus produce the elastic connective-tissue cushion termed the gum.

From the anatomical disposition of the pericementum conclusions may be drawn as to its physiological action. It is obvious that the relatively soft and elastic layer between the two bony formations — cementum and alveolus — is designed to lessen the concussion upon the jaw-bones during mastication. The oblique direction of the connective-tissue bundles is the most favorable for the suspension of the tooth within its socket, as the bundles correspond to the funnel shape of the socket, in the center of which is situated the conical root of the tooth. The elasticity of the layer of pericementum admits of a slight degree of motion of the roots; hence we understand the formation of facets on the proximate surfaces of the crowns of the teeth in crowded maxillary arches.

My specimens represent two varieties of pericementum — one of a reticu-

* "Manual of Dental Anatomy," Philadelphia, 1876.

† "Die antiseptische Behandlung der Pulpa-Krankheiten," Berlin, 1879.

‡ Extracted from the essay, "On Pericementum and Pericementitis." *The Dental Cosmos*, Philadelphia, 1879–80.

lar structure, termed myxomatous; the other is altogether fibrous. The myxomatous variety I have met with, as a rule, in young individuals. It consists of delicate fibers, or bundles of fibers in a net-like arrangement, which, in many instances, are supplied with round or oblong nuclei at the points of intersection. The meshes contain either a hyaline, apparently structureless, sometimes finely granular, basis-substance, or they hold plastids provided with a varying number of nuclei. The nearer to the cementum, the narrower is the myxomatous reticulum, and the smaller, therefore, are the inclosed plastids. The latter, in the immediate vicinity of the cementum, stand in more or less regular rows, entirely analogous to the bioplasson bodies around the developing bony tissue, known, since Gegenbaur, as "osteoblasts." Some of the meshes of the myxomatous tissue are considerably larger, and contain multinuclear bodies. Other meshes hold fat-globules, which, in specimens

FIG. 286.—PERICEMENTUM OF MYXOMATOUS STRUCTURE.

D, dentine; *C*, cementum of neck, *P*, pericementum; *M*, multinuclear body; *V*, capillary blood-vessel; *F*, fat-globule with a vacuole. Magnified 500 diameters.

preserved and hardened in a solution of chromic acid, very often contain closed spaces—so-called vacuoles. The myxomatous reticulum is traversed by numerous blood-vessels, mainly capillaries and veins, some of which can be seen entering the medullary spaces of the compact bone of the wall of the alveolus and in connection with the capillary system of the cancellous portion of the alveolus. I have met with but few nerve-fibers in my specimens. (See Fig 286.)

High amplification of the microscope plainly demonstrates the delicate, reticular structure of all plastids, the reticulum being visible not only in the contents of the meshes, but also within the fibers of the myxomatous reticulum. The latter feature is recognizable best on specimens deeply stained

with chloride of gold. The apparently structureless, or indistinctly granular, myxomatous basis-substance, held in the meshes of the myxomatous reticulum, proves to be a reticular structure, just as well as the bioplasson itself.

The second variety of pericementum is built up by fibrous connective tissue, which prevails in adults and persons of advanced age. The bundles of the fibrous connective tissue may be uniform in width throughout the whole pericementum, or there exists a zone of myxomatous or indistinctly fibrous character close around the cementum. The bundles are built up by a number of fibers which hold a varying amount of plastids—as a rule, more numerous the nearer to the cementum. On the latter there may be found rows of osteoblasts or scattered bioplasson bodies alternating with bundles of a delicate connective tissue, which are directly attached to the cementum. In a few instances I have seen rows of osteoblasts, the refracting power of which was considerably augmented. Such corpuscles looked shining and structureless, evidently on account of a deposition of lime-salts. The fibrous variety of the pericementum also contains fat-globules, sometimes in a surprisingly large quantity.

High magnifying powers of the microscope reveal a structure of the fibrous connective tissue, as follows: The fibers, a certain number of which combine in the formation of a bundle, are delicate spindles, directly connected with each other at their pointed ends. These spindles are separated from each other by a narrow layer of a light cement-substance. The interstices between the spindles are traversed in a vertical direction by extremely minute threads every way analogous to the thorns in the cement-substance surrounding epithelial elements. These threads, in many instances, are visible in specimens hardened by the chromic acid solution; they become very plain when thin sections have been immersed in a half per cent. solution of chloride of gold for one or two hours, or until the specimen has assumed a dark violet color. If the stain be complete, we also recognize that the spindles are not homogeneous, as they look in fresh, unstained specimens, but are rather traversed by a delicate, dark violet reticulum, the points of intersection of which are slightly thickened, and thus represent granules. (See Fig. 287.)

Between the spindles of the basis-substance plastids are seen—the so-called "connective-tissue cells." Some of these bodies exhibit shining, compact, oblong nuclei, with a certain amount of surrounding bioplasson, while others are devoid of nuclei, and split into spindle-shaped or polygonal lumps, which in size and shape fully correspond to the elementary formations of the fibrous basis-substance. In some instances, between the cementum and the osteoblasts there is interposed a small layer of fibrous basis-substance in the shape of delicate, slender spindles.

In its juvenile condition the pericementum represents a myxomatous connective tissue, the fibrous portion of which is comparatively scanty, while the bioplasson portion prevails. In this instance two varieties of basis-substance occur, viz.: the fibrous, building up the reticulum, and the myxomatous, filling a certain portion of the meshes. This condition arises from the indifferent or embryonal tissue, not only in the pericementum, but in all formations of connective tissue which, when fully developed, exhibit a fibrous structure. The only way to explain the formation of the myxomatous tissue is, that a part of the substance constituting the embryonal elements remains unchanged, a part is transformed into spindles of the myxomatous reticulum, and a part into myxomatous basis-substance.

The final result may be, especially in pericementum, either a jolly-like myxomatous, or a solid, fibrous basis-substance. The living portion, at all events, remains untouched by the chemical alteration of the lifeless fluid.

On this theory the transformation of the myxomatous tissue of juvenile into the fibrous tissue of adult age is easily explicable. We only need assume a dissolution or liquefaction of the already formed basis-substance in order to understand the reappearance of the embryonal condition at a certain stage of development. The myxomatous tissue as such never changes directly into a fibrous one, but must first be reduced into its embryonal or bioplasson condition, and from this in turn fibrous connective tissue may arise. The latter process is explained by the splitting and elongation of the plastids into spindles which become solidified; in other words, the lifeless fluid is transformed into a gluey basis-substance.

At no time has the reticulum of the living matter been interrupted or torn; the pericementum has never ceased to be a tissue either in its embryonal,

FIG. 287.—PERICEMENTUM OF FIBROUS STRUCTURE.

C, cementum of root; *PL*, pericementum, the fibers of which are built up by spindles, in longitudinal section; *PF*, pericementum, the elementary spindles of which are finer and cut obliquely; *P*[1], *P*[2], bioplasson bodies, either so-called connective-tissue corpuscles or so-called osteoblasts. Magnified 1200 diameters.

myxomatous, or fibrous condition. On the theory here explained, all changes in inflammatory processes of the pericementum may be easily understood.

(B) Pericementitis. Plastic Inflammation and New Formation. Practitioners are aware that pericementitis presents itself in two forms, evidently according to the intensity of the inflammatory process. One form is the plastic, which, if repeatedly recurring, leads to a new formation of connective tissue, the so-called hyperplasia, or hypertrophy; the other and more severe form is the suppurative pericementitis, which inevitably leads to a more or less extensive destruction of the pericementum, to death of the pulp, and not infrequently to necrosis of the alveolar process.

Pericementitis, in its mildest degree, with lower powers of the microscope, is recognizable by the presence of nests, filled with medullary elements, in

the midst of the connective-tissue bundles. The shape of these nests is, as a rule, oblong, corresponding to the longitudinal direction of the connective-tissue bundles, or roundish, in accordance with the cross-section of bundles. The scantier these nests, the milder is the inflammatory process. With high magnifying powers of the microscope, we learn that the earliest stage of the inflammation consists in a transformation of the connective-tissue fibers into bioplasson. (See Fig. 288.)

According to the spindle shape of the elementary fields of the basis-substance, spindle-shaped bioplasson bodies have appeared, wholly identical with the normal plastids within the fibrous connective tissue. All these bodies are separated from each other by light rims, and connected with each other by the delicate threads of living matter traversing those rims. The finely granular, newly appeared bioplasson bodies soon afterward become coarsely granular, which means that the living matter therein has increased in size.

FIG. 288.—INFLAMED PERICEMENTUM IN AN EARLY STAGE.

V, capillary blood-vessel, the endothelia of which are coarsely granular and proliferating; *M*, medullary or inflammatory elements, imbedded in a finely granular basis-substance; *S*, spindle-shaped elements. Magnified 1000 diameters.

We see next that a number of granules — the points of intersection of the reticulum — have increased in size to such an extent that they resemble small nuclei, and from these foci new elements are formed, partly shining and homogeneous, partly reticular in structure. After the originally solid lumps of living matter have split into a reticulum, many of the newly formed elements contain solid nuclei. All elements are uninterruptedly connected with each other by delicate threads of living matter. Thus, the inflammatory infiltration is established at first in the shape of scattered nests, the centers of which correspond to the capillary blood-vessels. In later stages almost the whole amount of the connective tissue is transformed into medullary elements to such a degree that only scanty bundles of the original connective tissue are left. The swelling of the pericementum accounts for the painfulness of the process; while the loss of the firm basis-substance and its replacement by medullary elements explain the looseness of the tooth. These features will also account for the peculiar sensation experienced by the patient that the tooth is raised out of its socket.

The largest accumulation of the inflammatory elements takes place in the immediate neighborhood of the blood-vessels, for in the middle of many nests capillaries can be traced. We readily understand that in the immediate vicinity of the source of nutrition the inflammatory process must be most active. This fact has been taken up as an argument by those who assert that the inflammatory nests are altogether due to an emigration of colorless blood-corpuscles. I am strongly opposed to this opinion, because my observations show that the majority of the inflammatory elements are originally connected

with each other by delicate threads, therefore representing a tissue. The endothelia of the capillaries share in the inflammation by being transformed into coarsely granular irregular bodies, which, by division, also produce new medullary elements, partly nucleated, partly devoid of nuclei. By the new formation of inflammatory elements from the endothelia the caliber of the capillary is first considerably narrowed and afterward completely lost. An exuberant growth of the endothelia will, as a rule, result in the destruction of the capillaries by suppuration, and will probably give rise to formations which I shall presently describe.

In most of my specimens of inflamed pericementum I have met with a singular formation. A number of medullary corpuscles coalesce into globular masses, greatly varying in size, and in some instances surrounding a central polyhedral space, evidently made by the compression of the former blood-vessel. The globular masses are either composed of medullary elements, shining, homogeneous, and split into smaller lumps of living matter, or they are continuous masses of a coarsely granular bioplasson, in which varying numbers of nuclei are seen. Formations of this kind are well known in inflamed periosteum and medulla of bone; they have been termed myeloplaxes, myeloid bodies, giant cells, etc.

My specimens plainly show that in the so-called plastic inflammation of the pericementum all inflammatory corpuscles remain connected with each other, and thus represent a medullary, embryonal, or indifferent tissue. In slight degrees of inflammation the morbid process may yield to what has been termed "the resolution of inflammation." Nothing is required but the re-formation of the basis-substance, and the normal condition is reëstablished. More severe forms of plastic pericementitis, or repeated recurrences of the inflammatory process, will result in a new formation of the connective tissue, the so-called hyperplasia.

Higher degrees of plastic pericementitis are invariably accompanied by inflammation of the gum, the cementum, and the bony alveolus.

Inflammation of the gum (ulitis, gingivitis) in its mildest form is marked clinically by the so-called œdema. Higher degrees of ulitis manifest themselves in essentially the same manner as pericementitis, viz.: first, the formation of scattered, afterward confluent, nests of inflammatory corpuscles. The origin of these nests from the connective-tissue bundles of the gum is exactly the same as in the pericementum.

Cementitis is shown under the microscope by the presence of bay-like excavations on the periphery of the cementum, and sometimes also beneath the surface. These excavations are filled with medullary or multinuclear bodies. To their presence is due the peculiar corroded appearance of the cementum on teeth extracted during an attack of pericementitis.

Osteitis on the bone of the alveolus is manifested by a dissolution of the basis-substance of the bony tissue, either in the shape of bay-like excavations corresponding to the territories of the bone-tissue, or in irregular fields filled with medullary elements penetrating from the surface into the depth of the bone. This process is invariably combined with osteomyelitis, and the result of both processes is the transformation of the hard, bony tissue into a soft medullary or inflammatory tissue. In some of my specimens of osteitis this change is exhibited to a very high degree, so that only small islands of bony tissue are left as remnants of the former wall of the alveolus.

Hyperplasia. An intense plastic pericementitis, or repeated attacks of a so-called subacute inflammatory process, will lead to a new formation of connective tissue, cementum, and bone.

Hyperplasia of pericementum occurs whenever a large number of inflammatory corpuscles are newly formed and remain in connection with each other, thus not ceasing to be a tissue. The inflammatory corpuscles in certain districts become elongated, and, after having split into spindle-shaped elements, are transformed into a solid basis-substance, which means a new formation of connective-tissue bundles. These bundles differ from those of normal pericementum in their greater density, and their very irregular arrangement. Hypertropied cementum is augmented in its whole bulk, and is built up by coarse bundles of connective tissue, between which, in the earlier stages of the hyperplastic process, more or less numerous nests of inflammatory elements are seen. In other instances, the whole pericementum is transformed into a dense cicatricial connective tissue, whose bundles are very small, and, by crossing each other in all directions, produce a felt-work. Hyperplastic pericementum, as a rule, holds fewer blood-vessels than the normal.

Sometimes scattered nests of the inflammatory corpuscles take up a high refracting power, which evidently is due to a deposition of lime-salts in them — the so-called calcification. This process is entirely different from ossification, though the former apparently precedes the latter. Scattered nests of inflammatory elements may be transformed also into clusters of fat-granules.

New formation of cementum is observable in two forms: either as re-formation in the bay-like excavations, or as a new formation on the outer surface of the cementum.

Re-formation of the cementum is always characterized by a deposition of lime-salts in the territories of the cement-corpuscles, previously dissolved by the inflammatory process. The bay-like excavations remain unchanged in their configuration, even after new cementum has formed. In the cementum of both the neck and the root I have met with such sharply circumscribed islands of newly formed cementum, apparently in no connection with the outer surface.

The inflammatory new formation on the surface of the cementum appears either in the shape of a continuous layer of cement-tissue, distinctly bounded toward the normal cementum, or jagged on the outer surface, with manifold elongations and erosions, filled with newly formed connective tissue. Sometimes relatively large globular formations appear on the outer surface of the cementum as the result of pericementitis.

There are globular bodies in connection with the cementum by means of a pedicle, which closely resemble those in the pulp-cavity attached to the dentine. These peculiar formations exhibit a distinct concentric lamination. They are surrounded by a layer of spindle-shaped medullary elements, and hold in their centers a radiating bioplasson mass, resembling a bone-corpuscle. As to their origin, there can be scarcely any doubt that they arise from clusters of medullary or multinuclear bodies, above described. All new formations on the surface of the cementum, caused by an inflammatory process, may be justly denominated "exostoses of the cementum." (See Fig. 289.)

I have repeatedly seen true bony new formations in hyperplastic pericementum. They appear in the shape of irregular islands or elongated spiculæ within the fibrous connective tissue, sometimes so near to the cementum that no doubt is left about their formation in the middle of the pericementum,

independently of the bony alveolus. These formations bear a close resemblance to embryonal bone — viz.: contain a large number of irregular bone-corpuscles with broad offshoots, and a comparatively small amount of bony basis-substance. On the periphery of isolated bony formations we can often distinguish the medullary elements (osteoblasts), which participate in the formation of bone by being partly transformed into basis-substance.

Lastly, true bony new formations may occur on the wall of the alveolus, which, after repeated attacks of pericementitis, as clinical observation teaches, is sometimes beset with thorny new formations of bone. These exostoses originate on the socket of the tooth from the medullary tissue, in the same manner in which exostoses grow on any other bone, as sequelæ of periostitis and osteitis. In the highest degree of development, such exostoses of the socket replace the pericementum to such an extent that only traces of the pericementum are left. No instance, however, at least to my knowledge, has been observed of a complete fusion of the socket with the tooth.

Pyorrhœa Alveolaris. Surgeons have long been aware of the fact that suppurative periostitis is the main, if not the only cause of necrosis of bone;

Fig. 289.—Globular Body, Result of Pericementitis.

G, concentrically striated mass, surrounded by small, spindle-shaped elements, holding a star-shaped bioplasson body in its center. *C*, cementum. *M*, multinuclear body, from which a globular body may originate; *IE*, inflammatory elements, crowded in the pericementum. Magnified 200 diameters.

thus, also, the consequence of suppurative pericementitis is necrosis of the alveolus, varying in accordance with the degree of the suppuration. No cure of the suppuration is possible until the necrotic parts of the bone have been eliminated from the body, either spontaneously or by surgical interference.

Under the microscope, the first stages of suppurative pericementitis are identical with those of the plastic form — viz.: there are nests of inflammatory corpuscles between bundles of unchanged connective tissue. The less, therefore, of this connective tissue is left, the more numerous the inflammatory elements are, the nearer is the tissue to suppuration.

With high magnifying powers of the microscope we see that the inflammatory process goes on in exactly the same way as in plastic pericementitis. The bundles of connective tissue are transformed directly into inflammatory corpuscles, which at first are all united with each other. This union is recognizable in relatively large nests, also, in which there are but scanty capillary blood-vessels left. It is only after the mutual connection of these elements is broken that the bodies, now isolated, deserve the name of pus-corpuscles, which are suspended in an albuminous fluid, and fill a cavity termed an "abscess." If a large number of inflammatory centers, which afterward become confluent all around the root of the tooth, have formed, we designate the disease "alveolar pyorrhœa."

In some of my specimens, among the inflammatory elements, there are seen capillary blood-vessels, containing a few colorless blood-corpuscles, some of which, by means of a slender pedicle, have penetrated the wall of the capillary, and are evidently engaged in emigration. These colorless blood-corpuscles, however, are finely granular, and, as such, easily distinguishable from the surrounding inflammatory corpuscles, the vast majority of which are coarsely granular or homogeneous. Emigrated colorless blood-corpuscles may share in the formation of pus-corpuscles, but the main mass of the latter is doubtless formed directly from the connective-tissue substratum of the inflamed part.

After the elimination of the pus the surrounding inflamed tissue grows in the shape of so-called "proud flesh" or granulations, which we not infrequently meet on the roots of teeth extracted during an attack of suppurative pericementitis, especially well developed in the bifurcations between the roots of molars. Such granulations are built up by a myxomatous connective tissue, which is freely vascularized, and, after having filled the cavity of the abscess, is transformed into a dense, fibrous connective tissue. This reparative tissue is termed a "cicatrix." Suppurative pericementitis will invariably heal by cicatrization.

Alveolar Abscess. This is a peculiar form of suppurative inflammation on the apices of the roots of teeth.

Examinations of microscopical sections through the root, the socket, and the alveolar abscess, demonstrate that the latter is either unilocular or multilocular, viz.: separated into two or several chambers, all filled with pus. The wall of the abscess is built up by a very dense fibrous connective tissue, the bundles of which mainly run a concentric course around the abscess, and are continuous with the unchanged or slightly inflamed pericementum higher up on the root. The sac is a product of plastic pericementitis, fully identical with what has been termed in former years the "membrana pyogena." When the inflammatory process has lasted for months, the newly formed connective tissue assumes a distinct fibrous structure, and between the bundles there are interspersed nests of inflammatory corpuscles. These may be partly transformed into fat-granules, or produce opaque layers in fatty degeneration. If, on the contrary, the alveolar abscess be of a more recent date, the fibrous structure of the sac is plainly marked on its periphery only, while the central portions bear the character of a myxomatous granulation-tissue. The strings or the septa traversing the abscess may, in accordance with the age of the disease, be found either of a fibrous or myxomatous structure. In both instances we often meet with a large number of newly formed capillary blood-vessels. The inner surface of the sac is not smooth,

but largely provided with irregular protrusions, or papillary outgrowths of a myxomatous structure, crowded with inflammatory elements. The sac contains inspissated pus, which, upon the cutting of microscopical sections, crumbles away.

Cementitis and osteitis always accompany an alveolar abscess. Cementitis leads to a destruction of the cementum in the shape of deep, irregular, bay-like excavations, which exhibit all stages, from the liquefaction of the basis-substance up to the transformation of the living matter into pus-corpuscles. Sometimes the excavations penetrate the dentine. In the highest degrees of pericementitis the apex of the root, inclosed in the alveolar abscess, is transformed into a thin, jagged, and corroded stump, with but scanty remnants of the former cementum.

Osteitis (inflammation of the wall of the alveolus) is an inevitable result of the formation of an alveolar abscess. The portion of the socket in contact with the sac of the abscess is widened, its surface being either smooth or jagged. Examination with the microscope leaves no doubt that the inflammatory elements, sprung from the bony tissue after dissolution of its lime-salts and liquefaction of its gluey basis-substance, become spindle-shaped, and participate largely in the formation of the wall of the abscess.

Literature. In regard to the literature of pericementum and pericementitis I have but little to say, as this subject has been very much neglected by nearly all histologists. I shall quote from a few only of the modern authors.

Carl Wedl* says: "Generally the root-membrane, or periosteum of the root, is of moderate density; the bundles of connective tissue forming it contain no elastic fibers, and inclose fusiform connective-tissue corpuscles; in addition to these, roundish elementary organs are met with."

According to E. Magitot,† "the root-membrane consists of two portions: an inner, which does not admit of being teased into fibrils; and an outer, lying near the alveolar wall, which has the appearance of a fibrous structure. The same writer also mentions the occurrence of 'cellules myéloplaxes,' similar to those found in the periosteum of bone, and cytoblastions (nuclei invested with a layer of protoplasm), which occur still more rarely." "The changes in the hard tissues of the root, which occur chiefly with chronic suppurating inflammation of the periosteum of the root, consist in necrosis and resorption, according to the nature of the tissue." "The histological appearances produced by the process of resorption are displayed in a manner similar to those which were observed in the resorption of the roots of the milk-teeth — *i. e.*, there are circumscribed depressions upon the outer surface of the cement, which are made up of groups of closely approximated, shallow, cup-shaped indentations. In the ridge-like elevations which bound the excavations well-preserved bone-corpuscles are to be found, while they become gradually less discernible in the deeper portions. Necrosis of the cement not infrequently is associated with resorption." "If the cement is entirely destroyed here and there by the suppuration, the dentine becomes similarly affected, and acquires a roughened or corroded appearance." "There are no indications of a vital action on the part of the dentine. The theories advanced to explain the manner in which the excavations are produced by resorption are mere suppositions; they may be regarded as induced either by the activity of the pus-

* "Pathology of the Teeth," Philadelphia, 1872. Page 59.

† "Mémoires sur les Tumeurs du Périoste Dentaire." 1868.

corpuscles, or by a fermentation process; with regard to the former, it is conceivable that the amœboid movements of the pus-corpuscles might wear away the dental substances; in the latter case, the generation of an organic acid might be assumed. In chronic cases, the eroded portions are covered by a thin membrane of connective tissue or by a layer of granulation tissue." "Sometimes, on the other hand, the inflammation spreads from the root-membrane to the socket of the tooth; when this occurs, the canals of the latter in the vicinity of the focus of suppuration become expanded; excavations, in the form of pits and grooves, are found in it, and, finally, there ensues a partial resorption of the alveolus, which process is induced by the proliferation of the elementary organs of the connective tissue." "In addition to the senile form, a hypertrophy occurs as a sequel of chronic affections of the root-membrane, consisting essentially in a thickening, and a more or less advanced callous formation. The generally straight bundles of fibrous tissue often pursue a radiating course for the most part — *i. e.*, they extend from the outer surface of the cementum toward the alveolar wall, forming a series of closely packed arches, and are inserted, by a fan-shaped expansion, into the osseous trabeculæ." "The bundles of connective tissue, especially in cases of very irregular hypertrophy, interlace one with another in various directions, forming a sort of felted work of bundles, which penetrate the enlarged foramina in the alveolar wall.

Charles S. Tomes * says: "The general direction of the fibers (of the alveolo-dental membrane) is transverse — that is to say, they run across from the alveolus to the cementum without break of continuity, as do also many capillary vessels; a mere inspection of the connective-tissue bundles, as seen in a transverse section of a decalcified tooth in its socket, will suffice to demonstrate that there is but a single 'membrane,' and that no such thing as a membrane proper to the root and another proper to the alveolus can be distinguished. At that part which is nearest to the bone the fibers are grouped together into conspicuous bundles; it is, in fact, much like any ordinary fibrous membrane. On its inner aspect, where it becomes continuous with the cementum, it consists of a fine net-work of interlacing bands, many of which lose themselves in the surface of the cementum. But, although there is a marked difference in histological character between the extreme parts of the membrane, yet the markedly fibrous elements of the outer blend and pass insensibly into the bands of the fine net-work of the inner part, and there is no break of continuity whatever. I have never seen the fibers, whether in longitudinal or in transverse sections, pass straight in the shortest possible line from the bone to the cementum, but they invariably pursue an oblique course, which probably serves to allow for slight mobility of the tooth without the fibers being stretched or torn."

Results. The results of my researches may be summed up in the following points:

(1) *Pericementum is a layer of connective tissue between the root of the tooth and the wall of the alveolus, and common to both. This connective tissue in the juvenile condition is myxomatous, rich in bioplasson bodies. In the adult it is fibrous, scantily supplied with plastids — the so-called connective-tissue cells. The bundles of the connective tissue are continuous with those of the gum and those of the periosteum of the alveolus.*

* "A Manual of Dental Anatomy," Philadelphia, 1876.

(2) *Inflammation of the pericementum is either a plastic (formative) or suppurative (destructive) process. These two kinds differ from each other only in degree and intensity.*

(3) *Plastic pericementitis is characterized by the formation of nests of inflammatory elements, arisen from medullary elements which have appeared from the connective tissue after dissolution of its basis-substance.*

(4) *Plastic pericementitis may terminate in resolution, if the inflammatory elements be not numerous, and the basis-substance be reëstablished; or it leads to hyperplasia of the connective tissue, if a large number of inflammatory elements have formed and the inflammatory process has repeatedly recurred.*

(5) *Pericementitis in its more intense degrees is always accompanied by cementitis of the root of the tooth, and by osteitis of the wall of the alveolus. Plastic pericementitis leads to a new formation of cementum, as well as of bone-exostosis.*

(6) *Suppurative pericementitis results from the breaking apart of the inflammatory corpuscles which have arisen from the connective tissue of the pericementum itself. Emigrated colorless blood-corpuscles probably share in the formation of pus-corpuscles; but no proof thereof is possible. The main mass of pus-corpuscles is due to a transformation and destruction of the inflamed tissue.*

CARIES. BY FRANK ABBOTT, M. D.*

Methods. The results recently obtained with regard to the minute structure of the teeth have been arrived at by *new methods*. As a matter of course, dried specimens of teeth, formerly almost exclusively in use, did not reveal any of the soft parts within the hard dental tissues. Only a frame of the tissue was left, and we may readily understand why the investigations of the carious process as yet have not passed above hypotheses and speculations.

For preparing dentine and cement, there is no better method known than slow decalcification by means of a one per cent. solution of chromic acid. The enamel of teeth prepared in the foregoing manner can never be cut, because it becomes extremely brittle; therefore, I was obliged to resort for its examination to the method first practiced by Dr. Bödecker. The thin slices should be kept for decalcification, for twenty-four hours, in a very dilute solution of chromic acid. A saturation of this solution of over one-half of one per cent., in my opinion, is deleterious to the enamel, which, if *completely decalcified*, shows only a *minute net-work* of *living matter*, as I first have observed, but no trace of the enamel-rods and prisms.

Caries of Enamel.† The clinical phenomenon of caries, in its very origin, consists essentially in a discoloration of the enamel. A whitish or grayish spot on the surface of the enamel is indicative, to an experienced eye, of the beginning of decay, which spot proves, when touched with an instrument, to be soft and crumbly. Often a brown spot is visible on the enamel as a sign of the softening process. The less pigmentation present, the more rapid is the process of decay. On the contrary, the more distinct the discol-

* Abstract from the author's essay, "Caries of Human Teeth." *The Dental Cosmos*, Philadelphia, 1878 and 1879.

† The fact that caries of the teeth begins as a chemical process scarcely will, in my opinion, be questioned. On a dead tooth, natural or artificial, as well as on teeth manufactured from the dentine of the elephant or the hippopotamus, the process will remain, under all circumstances, a chemical one, assisted only by the putrefying remains of the organic material of the tooth; while on a live tooth either acute or chronic reaction-changes take place.

oration, the slower is the softening process. Nay, dark-brown spots may be present in the enamel for many years without being followed by softening. The brown discoloration, as such, cannot be considered as an essential feature of caries of enamel, but it usually accompanies the carious process, and does so the surer, the slower the morbid process runs. On microscopic specimens we meet with decayed pits in enamel without any discoloration of this tissue. On other specimens we have a very marked orange or brown hue on the decayed part as well as in its neighborhood, and sometimes scattered specks are to be seen some considerable distance from the diseased part. The brown discoloration is located in the basis-substance of the enamel-rods, the outlines of which are much more marked than when in a healthy condition. The interstices between the rods here are plainly visible even with a magnifying power of only five hundred diameters. This power will reveal delicate beaded fibers of living matter within the interstices, which in healthy enamel can be seen distinctly with a power of eight hundred to one thousand only. Besides the discoloration, no material changes are seen on the enamel-rods.

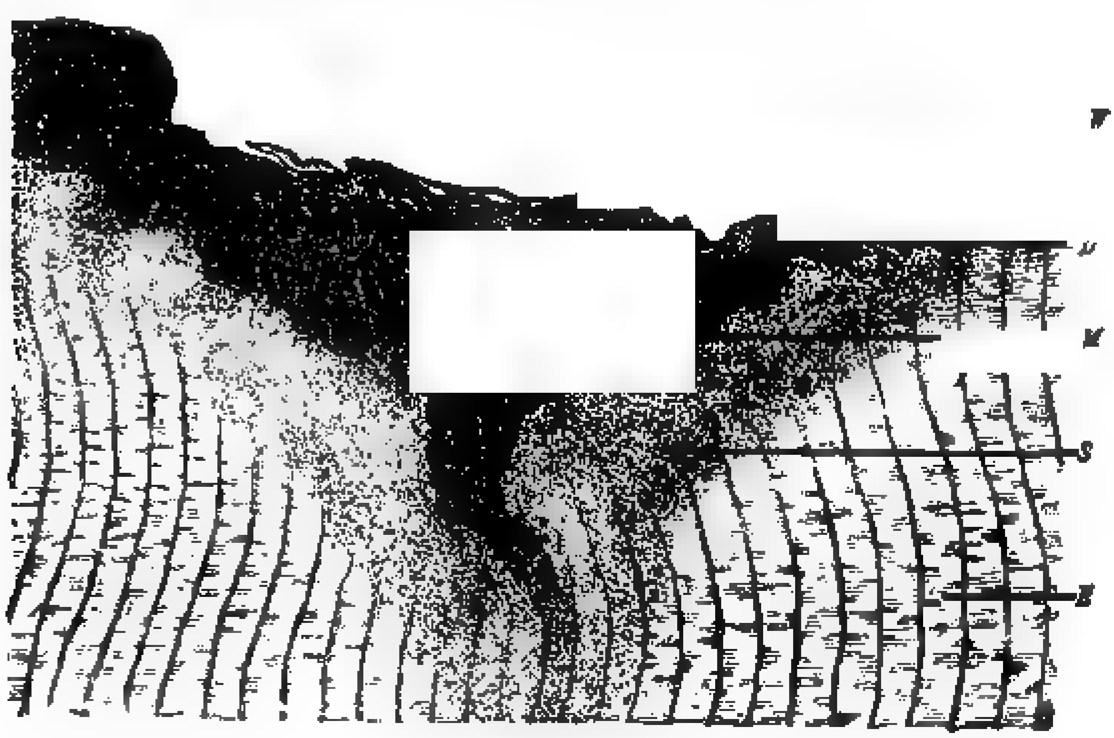


FIG. 290.—ACUTE CARIES OF ENAMEL.

E, unchanged enamel; *S*, enamel deprived of its lime-salts; *M*, enamel broken down to medullary corpuscles, *D*, medullary corpuscles, indistinctly marked; *N*, flat epithelia. Magnified 1000 diameters.

The process of decay in the enamel can best be studied on superficial erosions of the same, a sample of which I have illustrated. In this instance the brown discoloration of the decayed part was but trifling, and entirely absent in its vicinity, so that we have to consider it as a case of acute caries. Not a trace of micrococci or of leptothrix is visible in or above the decayed pit of the enamel, which again proves that these organisms do not play any important part in the process of caries. (See Fig. 290.)

The shape in which caries appears in the enamel is greatly varying. Besides the wedge shape, the forms in which caries proceeds are shallow or conical excavations, excavations with abrupt walls, fissures, and grooves. On the

bottom of the main excavation we sometimes see a smaller cavity, it being in a narrow or wide communication with the main decayed mass.

Besides the peculiar medullary elements forming the contents of a carious cavity of the enamel in its initial stage, I not very rarely have met with dark brown, irregularly shaped clusters filling the whole cavity. How such changes of medullary corpuscles are produced I am unable to say, although it seems to be kindred to the so-called *colloid* or *hyaloid* metamorphosis which we observe in other tissues, the only difference being that in caries the colloid clusters are deeply saturated with a uniform brown pigment.

Caries of Dentine. Sometimes the dentine, attacked by caries, looks but little changed on its periphery. A narrow zone of yellowish color forms the boundary toward irregular, shallow excavations. At other times, besides the bay-like excavations on the periphery, there are visible elongations, cylindrical, conical, pear-shaped, or leaf-like, passing down into the dentine in varying depths. There is no doubt that this form of decay of the dentine occurs with the least preliminary changes of the tissues; it evidently runs a slow course, and I think I am justified in calling this form of caries chronic. It seems evident that decay of a tooth assumes an acute or chronic form just in proportion to its perfect or imperfect calcification. Dead teeth in which

FIG. 291.—CHRONIC CARIES OF DENTINE.

D, dentine; *O*, the process of decay penetrating into the dentine in the shape of short offshoots, *C*, decayed mass. Magnified 200 diameters.

the pulps have been destroyed either by necrosis as a natural process, or by artificial means with caustics, very frequently run this kind of slow or chronic decay. (See Fig. 291.)

I have examined a piece of a hippopotamus tooth which for a period of about one year was worn in the mouth of a patient, and a spot became decayed about the size of a hemp-seed. On the bottom of the decayed pit numerous conical spots appeared running downward into the dentine, characterized by the absence of coloring matter in specimens stained with carmine. No material change besides was observable; even the dentinal canaliculi did not look enlarged. The bottom of the carious cavity was covered with a layer of finely granular, evidently disintegrated organic material, and above this the ordinary masses filling carious cavities in teeth, viz.: micrococci and leptothrix, were visible.

In chronic caries first the solution of the lime-salts of the dentine takes place, either along the bay-like excavations or in the shape of longitudinal

depressions. No reaction whatever follows this process. The glue-yielding basis-substance being deprived of its lime-salts, shows a yellow discoloration, and only traces of the dentinal canaliculi. The basis-substance then breaks down into an indistinct granular mass, which is immediately filled with a new growth of low vegetable organisms, viz.: micrococci and leptothrix.

My specimens plainly show that these organisms are not the *advance-guard* in the process of decay. The first change that takes places is exposure of the basis-substance by the chemical action of some acid, independent of the named organisms, which come to view only after complete disintegration of the basis-substance. I never have seen the penetration of these organisms into the dentinal canaliculi before a thorough decalcification of the basis-substance had taken place.

In the great majority of my specimens I have met with formations on the diseased boundary of the dentine which demonstrate a considerable degree

FIG. 292.—ACUTE CARIES OF DENTINE.

E, E, fissures in which the decay penetrates into the dentine; *I,* small islands of unchanged dentine. Magnified 200 diameters.

of reaction, produced by the irritating power of the same agent to which the lime-salts of the dentine yield. In fact, this was the case in all teeth which were alive when attacked by the carious process, or rather when removed from the jaws. On the boundary of this process we see irregularly shaped elongations running a certain depth into the tissue of the dentine. The more superficial the elongations are, the surer the morbid process may be termed a slow one; and, on the contrary, the deeper the elongations, the more certain we may be that the morbid process has advanced rapidly. The elongations mainly have the shape of fissures filled with a dark, granular material, if viewed with a low power. These fissures run independently of the direction of the dentinal canaliculi; nay, very often cross them. (See Fig. 292.)

On the surface of the carious portion of dentine we see irregular cavities

filled with the same granular mass that is present in the fissures, consisting evidently of débris of the former tissue, together, perhaps, with micrococci, and very often fine, thread-like leptothrix. The more rapidly the destruction of the dentine has advanced, the more irregular islands of dentine are left on the surface.

The outermost portion of the decayed part is, as a rule, brittle, and crumbles away in chromic acid specimens. Where it is left it shows a crowd of leptothrix and micrococci, without any distinctly recognizable remnants of the former tissue. On the boundary of the carious portion we, as mentioned above, meet with a yellow discoloration of the dentine, evidently produced by a chemical agent, which first dissolves out the lime-salts from the dentine, and in turn liquefies the glue-yielding basis-substance. In live teeth the yel-

FIG. 293.—CARIES OF DENTINE.

F, unchanged dentinal fiber. *P*, enlarged dentinal canaliculi, filled with bioplasson; *H*, medullary corpuscles in considerably widened dentinal spaces; *G*, complete transformation of dentine into medullary corpuscles. Magnified 1000 diameters.

low discoloration usually takes place in the shape of longitudinal strings of different diameters, running mainly parallel with the longitudinal direction of the dentinal canaliculi. Nay, we often see single yellow strings running from the bottom of a carious cavity in the enamel through the whole depth of the dentine to the pulp-chambers. While the unchanged dentine readily takes up the carmine, the strings, the deep yellow color of which is undoubtedly due to the action of the chromic acid, remain unstained. (See Fig. 292.)

We recognize, under the microscope, in longitudinal section of the dentine, that sometimes the yellow discoloration has taken place only within the limits of a few dentinal canaliculi, while at other times quite a number of these have undergone discoloration. Still sharper defined is the yellow discoloration on transverse sections. Here we see that mainly the canaliculi and their immediate neighborhood have taken up the yellow color in the shape of sharply circumscribed dots, which are the larger the nearer they approach to the periphery of the decayed part. The basis-substance between these yellow spots has taken up more or less carmine. (See Fig. 293.)

At a certain distance from the decay the canaliculi look unchanged, and each contains the central transverse section of the dentinal fiber, with its delicate radiated offshoots. Nearer to the decay we meet with moderately

FIG. 294.—CARIES OF DENTINE. OBLIQUE SECTION.

P, widened dentinal canaliculus, containing bioplasson; *N*, space containing medullary corpuscles; *M*, transformation of dentine into bioplasson, *C*, trace of dentinal canaliculus containing an enlarged fibril. Magnified 1000 diameters.

enlarged canaliculi, the center of which is occupied by a cluster of bioplasson, the granules and threads of which have readily taken up the carmine. One step farther we find the canaliculi considerably enlarged—to double or treble their original size—and they are filled with bioplasson, plainly exhibiting the net-like arrangement of the living matter. The most peripheral granules send delicate conical offshoots through the surrounding light space toward the unchanged basis-substance. In some of the enlarged canaliculi accumulations of living matter are seen fully in the shape of nuclei; sometimes two or more such nuclei may be seen surrounded by a varying amount of granular

bioplasson. Still nearer to the decay the canaliculi are enlarged to ten or fifteen times their original diameter, and the cavities thus produced are all filled with a partly nucleated bioplasson. Between the roundish cavities we meet with longitudinal cavities, arising from the confluence of several cavities in one main direction. The cavities continue increasing in size, and form large spaces, with rounded, bay-like boundaries, between which only scanty traces of unchanged basis-substance are left. Lastly, the basis-substance has entirely disappeared, and only bioplasson is visible in its place, either in the shape of multinuclear layers or of irregular so-called medullary elements, with rather faint marks of division. Nearest to the periphery the bioplasson does not exhibit any form-elements, but looks like a disintegrated granular mass, probably intermixed with or replaced by micrococci.

In less acute caries a relatively small number of dentinal canaliculi are enlarged and filled with bioplasson. The center of the bioplasson bodies is occupied by one or two nuclei, which look as if they originated from the former dentinal fiber. On the periphery of the dentine there are regular nests filled with bioplasson formations of the above description, partly broken down into medullary elements. On other parts, on the contrary, the transformation of the basis-substance into bioplasson has even preceded the changes of the dentinal fibers. The canaliculi are not noticeably enlarged; the dentinal fibers are either unchanged or slightly swollen, and more granular than in the normal condition; while outside these we have a thoroughly decalcified and liquefied basis-substance, which means a reappearance of the net-work of the living matter before the stage of disintegration. (See Fig. 294.)

Caries of Cement. So long as the gums are in their normal condition and position caries does not begin in the cement; but, if the gums have receded from any cause, thus exposing the cement which covers the necks of the teeth, it may then begin to decay. The microscope reveals a more or less advanced decay, which, in its essential features, is fully analogous to caries of the dentine when in a live condition. On the boundary of the caries we see, besides unchanged cement-corpuscles, those which have been enlarged and transformed into medullary or inflammatory elements. Nay, I have observed that the lacunæ holding the bioplasson body were partly unchanged while a part participated in the inflammatory process. (See Fig. 295.)

The enlargement of the cement-corpuscles is evidently not due to their direct swelling, but to a liquefaction of the surrounding basis-substance, in which the bioplasson condition, and with this also the medullary elements which have participated in the formation of the basis-substance, reappear. The inflamed portions of the cement look granular with lower powers of the microscope, but high powers reveal the net-like structure of the living matter and the formation of irregular polyhedral elements, which are separated from each other by a light, narrow seam, this being traversed by extremely delicate uniting threads.

Virchow's view that the bone-corpuscles swell and divide into inflammatory elements by being converted into proliferating mother-cells, is in my opinion wrong. No proliferation is demonstrable in the earliest stages of inflammation of the cement. Nothing but a decalcification, and thereafter a liquefaction, of the glue-yielding basis-substance takes place in order to bring to view the very same medullary elements which once have shared in the formation of the cement. The inflammatory reaction in the cement-corpuscle itself may be so slight that a part of this bioplasson may look almost unchanged, while

another part toward the decalcified basis-substance gives an appearance identical with that of the surrounding liquefied basis-substance. The result of this process is a transformation of the tissue of the cement into medullary or inflammatory elements. These remain in connection with each other by delicate threads of living matter, but at last become disintegrated, and give, together with micrococci and leptothrix threads, a decayed mass, just as well as enamel and dentine.

Results. I can sum up the results of my researches in the following aphorisms:

(1) *In enamel, caries in its earliest stage is a chemical process. After the lime-salts are dissolved out, and the basis-substance liquefied, the bioplasson reappears, and breaks apart into small, irregularly shaped so-called medullary or embryonal bodies.*

(2) *Caries of dentine consists in a decalcification, and in turn a dissolution,*

FIG. 295.—CEMENTITIS DUE TO CARIES.

C, unchanged cement-corpuscle; I, space filled with medullary corpuscles; P, cement-corpuscle, partly unchanged, partly transformed into medullary corpuscles; M, the cementum wholly transformed into medullary corpuscles. Magnified 1000 diameters.

of the glue-yielding basis-substance, around the canaliculi as well as between them. The living matter contained in the canaliculi is transformed into nucleated bioplasson bodies, which, together with bodies originating from the living matter in the basis-substance, form the so-called indifferent or inflammatory tissue.

(3) *Cement, if attacked by caries, exhibits first all phenomena known to be present in the early stages of inflammation of bone. The cement-corpuscles, as well as the basis-substance after its decalcification and liquefaction, produce indifferent or inflammatory elements.*

(4) *The indifferent elements originating through the carious process from enamel, dentine, and cement do not proceed in new formation of living matter, but become disintegrated and transformed into a mass crowded with micrococci and leptothrix.*

(5) *Caries of a living tooth, therefore, is an inflammatory process, which, beginning as a chemical process, in turn reduces the tissues of the tooth into embryonic or medullary elements, evidently the same as during the development of the tooth have shared in its formation; and its development and intensity are in direct proportion to the amount of living matter which they contain, as compared with other tissues.*

(6) *The medullary elements, owing to lack of nutrition and to continuous irritation, become necrosed, and the seat of an active new growth of organisms common to all decomposing organic material.*

(7) *Micrococci and leptothrix by no means produce caries; they do not penetrate the cavities in the basis-substance of the tissues of the tooth, but appear only as secondary formations, owing to the decay of the medullary elements.*

(8) *In dead and artificial teeth, caries is a chemical process, assisted only by the decomposition of the glue-yielding basis-substance of dentine and cement.*

History. John Hunter* says: "The most common disease to which the teeth are exposed is such a decay as would appear to deserve the name of mortification. But there is something more, for the simple death of the part would produce but little effect, as we find that teeth are not subject to putrefaction after death, and therefore I am apt to suspect that during life there is some operation going on which produces a change in the diseased part."

Joseph Fox† says: "The diseases to which the teeth are subject are similar to those which affect bones in general, and in like manner they have their origin in inflammation. The teeth differ only from bones in not possessing sufficient living power to effect the process of exfoliation."

Thomas Bell,‡ under the heading of "Gangrene of the Teeth, commonly called Caries," says: "The most common disease to which the teeth are liable is that which has hitherto been universally known under the name of *caries* —a name which, although authorized both by English and Continental writers, is in this instance totally misapplied. It is, in fact, calculated essentially to mislead, as the disease has not the slightest analogy to true caries of bone." "Still, however, the true proximate cause of dental gangrene is inflammation. That the bony structure of the teeth is liable to inflammation appears not only from the identity of the symptoms which take place in them, when exposed to causes likely to produce it, with those which are observed in the other bones when inflamed, but more conclusively still from the fact, already mentioned, that teeth are occasionally found in which distinct patches, injected with the red particles of blood, have been produced by this cause after the continuance of severe pain."

Dr. E. Magitot,§ in his general conclusions, says: "Dental caries is a purely chemical alteration of the enamel and ivory of the teeth. Lesions of the enamel consist, after the removal of the cuticle, in a purely passive chemical disorganization of the prisms composing its tissue. Lesions of the

* "Diseases of the Teeth," etc., 1778.

† "The History and Treatment of the Diseases of the Teeth and Gums," 1806.

‡ "Anatomy, Physiology, and Diseases of Teeth," 1831.

§ "Treatise on Dental Caries" (English translation by Dr. T. H. Chandler, 1878).

ivory, consisting likewise in a chemical decomposition of its elements, may sometimes, though rarely, remain passive; but most frequently they determine in the tissue phenomena of reaction that manifest themselves by the appearance of a cone or white zone, formed by a mass of canalicules obliterated in consequence of a formation of secondary dentine. The tooth attacked by caries does not remain passive and inert, but may in some measure undertake to resist its action by the phenomena of condensing dentification of the ivory. The agent of dental caries is the saliva, become the medium of acid fermentation or the vehicle of foreign substances susceptible of altering directly the tissues of the ivory and the enamel. The intimate mechanism of the production of caries is a simple solution of the mineral and calcareous salts which enter into the constitution of the enamel and of the ivory, by the agent of new formation."

Leber and Rottenstein * say: "The action of acids alone does not account for all the phenomena which appear in caries of the teeth. The acids attack first the enamel and rapidly change it to a chalky mass; later on their action is felt in a marked manner upon the dentine, which becomes more transparent, and, in fine, as if cartilaginous, by the very slow, but progressive loss of its calcareous salts. Caries, on the contrary, proceeds slowly in the enamel; it is much swifter in the dentine, where it proceeds promptly along the canaliculi. This difference of progress must be attributed to the participation of the fungi in the work of the caries. The elements of the fungus glide easily into the interior of the canaliculi, which they *dilate*, and thus favor the passage of the acids into the deeper parts; these same elements cannot penetrate a compact enamel, or at least they enter more slowly, and only when the elements which form it have been greatly changed by the action of acids. . . . For them (the leptothrix) to be able to penetrate thus, it is necessary that the teeth be in a suitable condition; the enamel and the dentine must have lost their density by the action of acids."

Carl Wedl † says: "It was quite natural to transfer to the teeth the signification implied in the expression 'Caries of bone;' indeed, the fundamental phenomena, namely, the destruction of the hard tissues, offered a striking analogy. In their development, however, the two processes by no means present such an identity. Caries of bone, as is well known, is an inflammatory process (osteitis) which originates in the soft parts of the bone and erodes its hard tissue. This is not the case with the carious process in the teeth, which commences in the hard tissues and spreads to the vascularized and nervous dental pulp. In sections made in a direction transverse to the axis of the radiating dentinal canals, a greater or less number of canals are met with whose limiting walls (the so-called dentinal sheaths) describe unusually large circles, and whose cavities are replete with a mass which has in some places a homogeneous, in others a molecular appearance, and forms convex projections beyond the surface of the section. The transverse diameters of the widened and filled canals vary, some being at least three times as large as others. The intertubular tissue presents a *molecular cloudiness*, and is beset with grains having the appearance of fat. . . . Since we know that an interchange of material takes place in the dentine and cement during life, as is proved by the occurrence of atrophies, hypertrophies, and new formations, and that the dentine possesses a degree of sensibility, we cannot reject absolutely the idea of a reaction on the part of both hard tissues against the effects of external agents. Some

* "Dental Caries and its Causes," 1873.

† "Pathology of the Teeth," 1872.

authors seem to have had an intimation of this idea, since they were inclined to consider the textural changes in carious dentine as vital processes. There can be no doubt that the sensibility, sometimes increasing to actual pain, of the dentine, when deprived of its protecting covering, is a vital action, and that this becomes diminished when the most sensitive, the peripheral portion, is destroyed by an external agent. These facts, however, are by no means sufficient to enable us to draw a conclusion in favor of the reactionary power of dentine in parts which are attacked by caries. In consequence of the decomposition of the secretions, acids are formed which extract the calcareous salts from the hard tissue, and give rise to a disintegration of the affected portions of the latter, in which no inflammatory reaction occurs."

Tomes* says: "Although dental caries has been investigated and described by all who have written upon the subject of Dental Surgery, from the earliest period when disorders of the teeth first attracted attention down to the present time, yet it can scarcely be said that the nature of the disease is perfectly understood, for even now two hypotheses prevail. In one the disease is assumed to be no disease whatever, but merely the result of chemical solution of the dental tissues, and therefore dependent both in its origin and its progress on the uncontrolled action of physical and chemical laws. According to the other hypothesis, the fact that teeth are part of a living organism, if not essential to the origin of the mischief, at all events profoundly modifies its progress. . . . Caries is an effect of external causes in which so-called 'vital' forces play *no* part."

The *processes concerned in the destruction of the temporary teeth* were studied in my laboratory by Frank Abbott, but the result is not yet ready for publication. The bay-like excavations observed in the cement and the dentine are due to a dissolution, first, of the lime-salts, and afterward of the basis-substance, which causes the reappearance of bioplasson in certain pre-formed territories. The new infiltration of these territories with basis-substance often results, even in the dentine, in a formation of bone-tissue, and it is probable that the same process takes place in the enamel also. How much of the erosions, which are visible in these structures, is due to a growth of granulation tissue into the dental tissues from without, has not yet been positively determined.

The *development of the teeth* has for a number of years been studied in my laboratory by C. F. W. Bödecker, and these studies are not yet completed. One of the important facts gained by the researches of Bödecker is, that the views held by former observers, concerning the development of the enamel, is erroneous. It is true that the enamel starts as an epithelial prolongation of the oral cavity, but the epithelia themselves never participate in the formation of enamel. The epithelia

* "System of Dental Surgery," 1873.

break down into medullary corpuscles, from which arises the well-known graceful myxomatous tissue. This tissue again returns to the medullary condition before producing enamel, the process being identical to that by which dentine is produced. Dentine is formed of medullary corpuscles, which are arranged in rows at the periphery of the papilla, and which afterward change into the glue-yielding basis-substance, the seat of infiltration, with lime-salts. The canaliculi of the dentine are formed *between* the medullary corpuscles, and the dentinal fibers arise from a coalescence of the living matter which is present *between* the medullary corpuscles, termed "odontoblasts."

XVII.

THE LIVER.

THE LIVER, the largest gland of the body, is neither acinous nor tubular, but has a peculiar structure of its own. Its vascular supply is predominantly venous, and is obtained from the portal system. From this blood the epithelia elaborate a secretion, the bile, which does not exist as such in the blood.

Corresponding with the lobate shape of the liver, which, however, is nowhere very distinctly marked, the intimate structure of the liver is lobular, though in man and in most mammals the lobules also are not sharply defined, but in many places appear confluent. In the pig's liver the single lobules are easily discerned with the naked eye. The lobules are composed of epithelia and capillary blood-vessels; they are inclosed in fibrous connective tissue, called the interstitial tissue, which is more abundant in some places than in others, and in many localities is altogether lacking. Around the lobules, in the interstitial connective tissue, run branches of the portal veins, of the hepatic artery, the bile-ducts, the lymphatics, and the larger bundles of nerves. In the lobules, capillaries are found which are derived from veins, and which carry, therefore, only venous blood; while the center of each lobule is occupied by the hepatic vein. The system of the portal veins is arranged at right angles to the system of the hepatic veins. Where the portal veins are cut longitudinally, the hepatic vein appears in transverse section, and *vice versa*. (See Fig. 296.)

The portal vein, upon entering the hilus of the liver, divides into smaller veins, which ramify in all directions, only the

larger branches being surrounded by connective tissue. Between the lobules the portal vein ramifies into smaller veins, which subdivide into capillaries. The latter arise either from one portal vein, which supplies the neighboring lobules with capillaries, or from two parallel veins, running in a curved direction corresponding with the peripheries of two neighboring lobules. These veins, which are connected by transverse ramules, split up into numerous capillaries for the supply of the lobules. The vessels

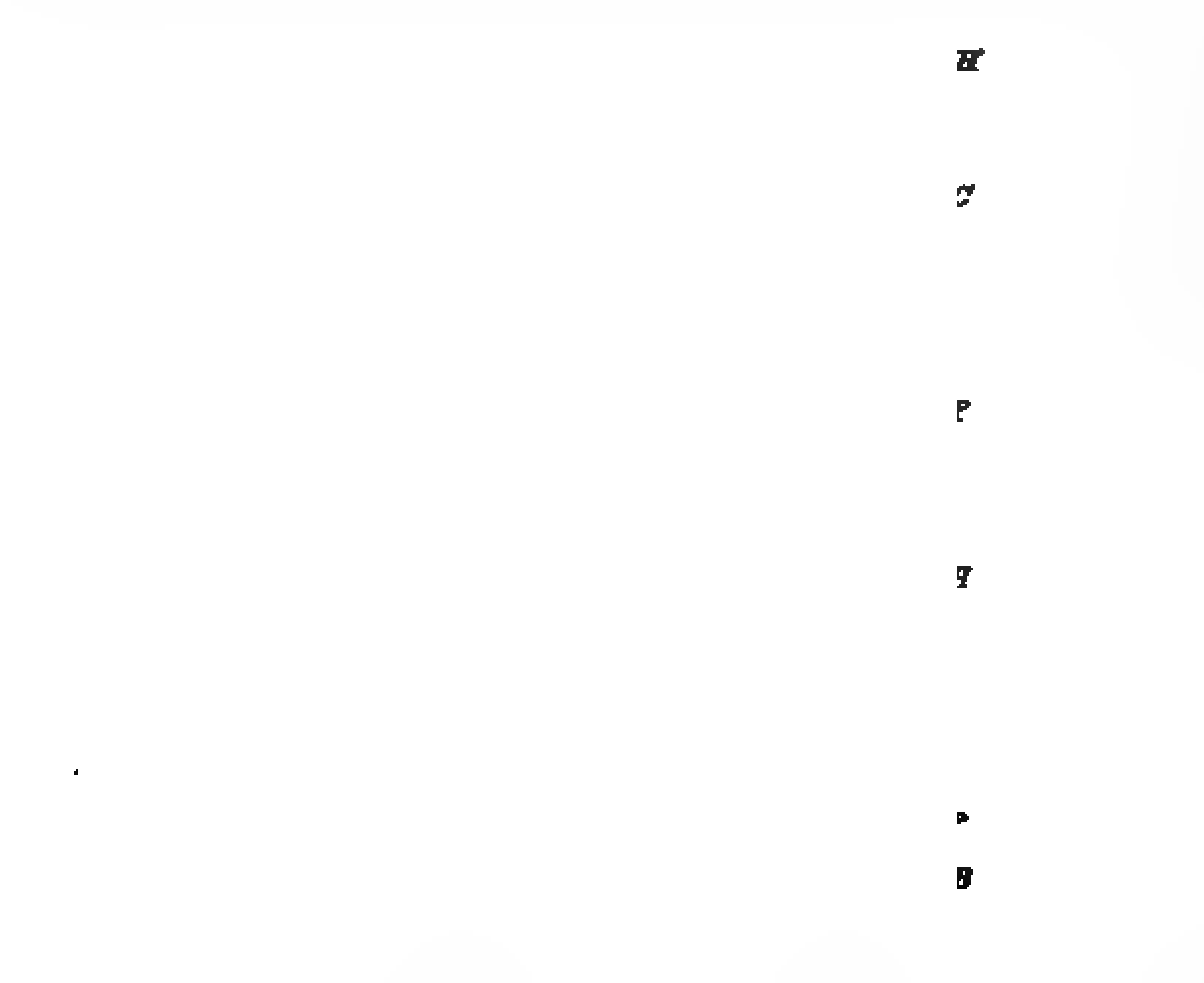


Fig. 296.—Liver of a Cat. Injected.

P, P, branches of the portal veins, partly surrounded by interstitial connective tissue; *C*, capillaries of the lobules; *H, H*, central hepatic vein; *B*, bile-duct. Magnified 100 diameters.

bordering the lobule are frequently capillary formations, especially in those parts where a larger amount of interstitial connective tissue is present.

The capillaries of the lobule are very wide and slightly sinuous. We never meet with a uniform distribution of capillaries throughout the lobule, for between wide capillaries narrow ones are invariably found, frequently separating a group of epithelia by their

endothelial walls, which are arranged in close contact, without a marked caliber. This disposition of vessels is, as a matter of course, less noticeable in injected specimens than in those taken from livers which are simply hardened. From this fact we may infer that the capillary system of the lobule is never completely filled with blood; and if the blood-supply at one surface of an epithelium is abundant, the capillary at the opposite surface is closed. It is also admissible to suppose that, by the enlargement of a number of epithelia, during their secretory action, some capillaries are occluded; or lastly, it may be that new capillaries are forming in the lobules of the liver during the whole life of the individual.

The capillary meshes are extremely narrow, so that there is never room for more than two complete epithelia between two capillaries. We often find, where the capillaries exhibit a radiating arrangement, rows of epithelia lying between them; and the appearance of these epithelial rows is caused by the occlusion of transverse capillaries which connect the longitudinal vessels. The transverse capillaries in such cases can be recognized by their endothelia with high powers of the microscope only. As a rule, therefore, one half of the epithelial circumference will be supplied with blood, although a greater portion may be encircled by capillaries. (See Fig. 297.)

FIG. 297.—LIVER OF A CHILD.

C, capillary blood-vessels, partly gaping, partly occluded, holding in their meshes the liver epithelia; *B*, bile-capillary (*t*), cut transversely. Magnified 500 diameters.

The center of a lobule holds the *hepatic vein*, which arises as an abrupt widening from the confluence of the capillaries. It is surrounded by a very small amount of connective tissue, has no muscle coat, and is never accompanied by bile-ducts or arteries. The hepatic veins, which always occupy the centers of the lobules, unite into somewhat larger branches, which are most marked on the posterior portion of the liver, and are called *sublobular veins*. By the union of these the hepatic veins proper originate.

The term "interlobular veins" is used to designate the portal branches lying between the lobules, and the term "intralobular veins" the central hepatic veins. These denominations are, however, superfluous and easily confounded.

The rows of the liver epithelia, as mentioned before, may be either single or double—*i. e.*, there may be a capillary blood-vessel on either side of the epithelium, or the epithelia may lie close together in one capillary mesh. In places where the capillaries run in a prevailing longitudinal direction, this relation is not well marked, as the epithelia overlap the capillaries on all sides; while, in places (see Fig. 299) where the capillaries are cut transversely, their relation to the epithelia—these being arranged wreath-like around the blood-vessel—is plain. (See Fig. 300.) Some authors claim that there is never more than one epithelium in a capillary mesh; if this were true, the small openings at the corners of neighboring epithelia (marked *B* in Fig. 297) would have to be considered transverse sections of very narrow or occluded capillaries, and not bile-capillaries. In the human liver it is impossible to decide in every instance whether a minute transverse section in the middle of an epithelial group is a narrow capillary blood-vessel or a bile-capillary. Much confusion has been caused, especially in the description of morbid processes, by the inability of positively discriminating between the two above-named formations. Those who claim that the bile-capillaries have an endothelial investment certainly must have mistaken capillary blood-vessels for them.

The *liver epithelia* form a continuous layer around the capillary blood-vessels, although in thin sections their continuity appears interrupted by the calibers of the capillaries. In the human liver the single epithelia are cuboidal, irregularly polyhedral; in the rabbit's liver, more or less hexagonal. They exhibit one or two nuclei; the latter condition being rarer in the human than in the rabbit's liver. In the nuclei, as well as in the body of the epithelia, the reticular bioplasson structure is visible, as seen in all living elements of the tissues, including the epithelial. The liver epithelia are separated from each other by a light, narrow rim of cement-substance which is traversed at right angles by extremely delicate filaments, identical with the so-called "thorns" or "prickles" met with in other epithelial formations. These features were discovered in my laboratory by H. Chr. Müller. The bile-capillaries are simply excavations in the cement-substance. (See Fig. 298.)

The meshes of the bioplasson reticulum of the liver epithelia, shortly after administration of fatty food, contain fat-granules and sometimes brown pigment-granules (of the bile?), especially in the vicinity of the bile-capillaries; a diffused brownish pigment is invariably present. The cement-substance holds, as will be shown later, the terminal nerve-fibrillæ. At the border next to the capillary wall a light rim is visible, traversed by delicate filaments, which directly unite the bioplasson reticulum of the epithelium with that of the endothelial wall of the capillary.

FIG. 298.—LIVER EPITHELIA OF THE RABBIT. [PUBLISHED BY H. CHR. MÜLLER IN 1876.]

CS, cement-substance between the epithelia; *BC*, bile-capillary excavated in the cement-substance. Magnified 1200 diameters.

The *bile-capillaries* were first described by J. Gerlach, and, as mentioned before, are excavations in the cement-substance between the epithelia, always at the surface of the epithelium, opposite to the place which comes in contact with the capillary—the point, therefore, of the least pressure. By some authors they are termed intra-lobular bile-vessels, while those called the inter-lobular bile-vessels, and running between the lobules of the liver, correspond to the bile-ducts. The bile-capillaries are destitute of an epithelial investment, and are also without a structureless wall of their own. Their location being between two neighboring epithelial surfaces (see Fig. 298), a portion of the bile-capillary is surrounded and enclosed by the cement-substance, while other parts of its circumference are in direct communication with the interior of the adjacent epithelia—that is, with the meshes of the bioplasson reticulum. Thus, it becomes intelligible that, by an active contraction of this reticulum, the newly formed bile is forced into the place of the least resistance and pressure—*i. e.*, the bile-capillary.

Successful injections of colored gelatine into the bile-capillaries, by E. Hering, prove that in the rabbit's liver all these vessels pursue a course corresponding to the middle of the epithelial surface, and I can, from my own observations, corroborate the statements of Hering. In the top view, the hexagonal epithelia appear to be surrounded by a rim of injected colored material, and it is only the darker dots in the middle of a colored line, corresponding to the middle of an epithelial sur-

face, which indicate the location of the bile-capillaries. In places where the blood-capillaries are cut transversely, most of the bile-capillaries will also appear as darker dots between those surfaces of neighboring epithelia which are most distant from the parts that are in contact with the capillaries. (See Figs. 299 and 300.)

FIG. 299.—RELATION BETWEEN THE CAPILLARY BLOOD-VESSELS AND THE EPITHELIA, IN A LONGITUDINAL DIRECTION. LIVER OF A RABBIT. BILE-CAPILLARIES INJECTED.

E, liver epithelia; *B*, bile-capillaries; *C*, capillary blood-vessels. Magnified 1000 diameters.

FIG. 300.—RELATION BETWEEN THE CAPILLARY BLOOD-VESSELS AND THE EPITHELIA, IN A TRANSVERSE DIRECTION. LIVER OF A RABBIT. BILE-CAPILLARIES INJECTED.

E, liver epithelia; *B*, bile-capillaries. *C*, capillary blood-vessels. Magnified 1000 diameters.

In the liver of the cat the relations of the bile-capillaries to the epithelia are somewhat different, inasmuch as the capillaries run both along the surfaces and the edges of the epithelia (see Fig. 302). In the liver of man most of the bile-capillaries run along the edges of the epithelia, and to this is due the appearance of the small, light apertures, which are seen at the point where three or four epithelia meet (see Fig. 297). The difficulties in discriminating between occluded blood-capillaries and bile-capillaries I have before alluded to. Should the conception be correct, that several liver epithelia lie around a central bile-capillary, while the opposite broad surfaces of the epithelia are in contact with the blood-vessels, a tubular arrangement of the liver epithelia might become admissible. Some authors have

already claimed that the liver of man can be classified among the tubular glands (Biesiadecki). In human embryos these relations are still more marked, and for this reason Toldt and Zuckerkandl have maintained that the structure of the liver of human embryos is tubular, each bile-capillary being surrounded by from three to five liver epithelia; the transformation into liver-structure proper begins, according to these authors, after birth. But, in fact, there is no difference between the liver of an embryo, that of a child six years old (see Fig. 277), and that of adults, with the exception that the individual epithelia appear larger with the advancing development of the liver. (See Fig. 301.)

FIG. 301. — LIVER OF A HUMAN FŒTUS OF FIVE MONTHS.

E, epithelia, arranged around a central bile-capillary: *C*, capillary blood-vessels, containing a few blood-corpuscles, their endothelial wall detached from the surface of the liver epithelia. Magnified 500 diameters.

In places where interstitial connective tissue is most abundant, the bile-capillaries, upon approaching the periphery of a lobule, produce a system of canals lying between the outermost epithelia and the connective tissue, and inosculating with the *bile-ducts*. These at first are only slightly larger than the bile-capillaries, and by their union at right angles produce larger tubules, which invariably run in the interstitial connective tissue only. The epithelial lining, at first composed of flat and small bodies, gradually becomes more distinct, assuming the characters of cuboidal epithelia, while in the largest ducts the epithelia are distinctly columnar. Toward the central caliber the cement-substance produces a distinct investing layer, which in the larger ducts is studded with short rods (Virchow), similar to those of the columnar epithelia of the intestines. In the smaller ducts the connective tissue is not differentiated into a separate investing layer, while the larger ducts have such a layer, provided with elastic fibrillæ and a reticulum of capillary blood-vessels; smooth muscle-fibers are also met with in the wall of the larger bile-ducts. (See Fig. 302.)

E. H. Weber has described as *vasa aberrantia* bile-ducts which occur, sometimes in large numbers, in membranaceous formations on the outside of the liver-tissue, where, evidently, in the

more advanced stages of development of the liver an atrophy of the tissue had taken place. Such formations are found at the free border of the left lobe, in the neighborhood of the portal vein, near its entrance into the porta, and in the connective tissue surrounding the gall-bladder. These bile-ducts in some parts show very wide calibers, and in others are in the process of obliteration and transformation into connective tissue.

The *interstitial connective tissue* is more abundant the nearer it is situated to the porta of the liver; it is in direct connection with the connective-tissue layer of the peritoneum, which, in this

P

BD

G

BC

FIG. 302.—BILE-CAPILLARIES, UNITING INTO BILE-DUCTS. INJECTED LIVER OF A CAT.

G, interstitial connective tissue; *P*, portal vein, branching into capillaries, *C*; *BC*, bile-capillaries, *BD*, bile-duct. Magnified 1000 diameters.

locality, bears the superfluous name of Glisson's capsule. In it we meet with large veins, all of which are necessarily portal; with arteries,—viz.: the branches of the hepatic artery,—and with capillaries and lymphatics. We find transverse and longitudinal sections where the union of the smaller with the larger ducts takes place. The smaller ducts often lack a distinct bore, evidently from being compressed; while the larger ducts, having a distinct lining of columnar epithelia, always exhibit a distinct circular caliber. (See Fig. 303.)

At the whole periphery of the liver the interstitial connective tissue is in connection with the peritoneal capsule. Besides, there is also a slight amount of connective tissue said to accompany the capillary blood-vessels within the lobule.

The larger bile-ducts are composed of fibrous connective tissue, in which numerous acinous or racemose mucous glands are imbedded. These glands, especially in the larger vasa aberrantia, exhibit the currant-like shape, and are arranged in regular double rows along the longitudinal axes of the ducts.

The *gall-bladder*, as well as the three largest bile-ducts, are lined by a connective-tissue layer abundantly supplied with

FIG. 303.—INTERSTITIAL TISSUE OF THE LIVER OF A CHILD, NEAR THE PORTA.

G, fibrous interstitial connective tissue – so-called Glisson's capsule; *P*, portal vein, *C*, capillary blood-vessel; *D*, *D*, bile-ducts cut in longitudinal and transverse directions; *A*, artery in transverse section; *L*, lymphatic. Magnified 500 diameters.

blood-vessels forming ridges in the bladder. Next to this follows a layer of smooth muscle-fibers, which freely interlace, and the outermost layer blends with the structure of the covering peritoneum. The inner lining consists of columnar epithelia, which are prolonged to form mucous glands (Luschka).

The *hepatic artery* is, in comparison with the size of the organ it supplies, a small vessel, entering the porta with the portal veins.

Its branches are found only in the interstitial connective tissue (see Fig. 303). It furnishes the capillaries around the larger portal veins and bile-ducts, and those supplying the outer capsule of the liver. The capillaries of the interstitial tissue are said, by some authorities, to inosculate directly with the capillaries of the lobule; while others maintain that small veins arise from the interstitial capillaries and unite with the portal veins.

The *lymphatics of the liver* are found in moderately large numbers in the interstitial tissue and in the capsule. A portion of these vessels leave the liver at the porta, where they form a plexus around the portal veins and the hepatic artery, and another portion issue from the periphery through all peritoneal reduplications, which unite the liver with the adjacent organs. The lymphatics have everywhere endothelial walls of their own. Von Wittich succeeded in injecting the lymphatics of the liver by forcing a concentrated solution of indigo-carmine into the trachea of rabbits recently killed by exsanguination. He saw, besides the above-mentioned plexuses, other plexuses around the hepatic veins, and claims that from the interlobular lymphatics prolongations pass into the lobules between the capillaries and the liver epithelia.

The Termination of the Nerves in the Liver.

By M. L. Holbrook, M. D.*

As the best histologists have maintained that our knowledge of the termination of the nerves of the liver is very slight and imperfect, I have undertaken, by a careful and extended series of researches, to throw some light on the subject. I have examined livers from the following animals: the dog, cat, woodchuck, owl, crow, hawk, and the ox. I have also examined the livers of a child and of an adult. The methods which I have employed have been the simple carmine-staining of specimens preserved in chromic acid, staining with picro-carmine, osmic acid, and chloride of gold. None of these reagents proved of much value, except the chloride of gold. The use of osmic acid, so highly praised by some observers, in my hands gave no satisfactory results, for, though it makes medullated nerves plainly visible by rendering them black, it has scarcely any effect on non-medullated nerves, and it is these which are to be found in the liver in a far greater number than medullated nerves. Chloride of gold, as usually employed, also failed to give any good results, but in combination with formic acid they were very satisfactory. The suggestion of a combination of chloride of gold and formic acid I learned from Löwitt,† and my method of employ-

* Printed in abstract from the author's manuscript.

† "Die Nerven der glatten Musculatur." Sitzungsber. d. Wiener Akad. d. Wissensch. lxxi. Bd.

ing it was as follows: Pieces of the fresh liver—best that of man or the ox—are frozen in a microtome and cut into thin sections. These are next placed in a half per cent. solution of chloride of gold for thirty to forty minutes. After this it is immediately washed carefully in distilled water, and at once subjected to formic acid of a specific gravity of 112 from five to eight minutes. The thinner the sections the less time is required for the acid to act upon them. Immediately after their removal from the formic acid they must be again thoroughly washed in distilled water and exposed to the light, and then mounted in glycerine.

The place most favorable for finding nerves is the *porta*. In the ox, in the region where the large vessels enter the liver, there is considerable fibrous connective tissue, in which numerous bundles of mostly non-medullated nerves may be seen coursing in the interstices between the bundles. I have succeeded best by taking sections from a portion of liver immediately bordering on the hepatic artery, a few inches from its entrance into the organ, or some of its branches. I am also of the opinion that the best sections are made by placing the material in the microtome in such a manner that the sections are cut vertical to the artery.

The nerves are marked by a large number of nuclei, by the presence of a delicate sheath of perineurium around each fiber, and by the dark violet color they had taken on from the treatment before described.

On the border of the lobules the nerves, which were still in bundles of from three to five, sometimes more, ramified and entered the lobules in different places, mostly branching at acute angles along the capillary blood-vessels. As I have traced the nerves entering the lobule to their connection with the bundles of nerves between the lobules, no doubt can arise as to the nature of the fibers which I have seen. Such fibers are to be found in the interlobular connective tissue distant from the porta, as well as in the connective tissue of the porta itself. Unquestionably, therefore, the nerves pass into the lobules and ramify along the capillary blood-vessels. This assertion is based on the fact that the ramifying nerves were always seen running in the light interstices between the liver epithelia, which, as we know, are occupied by capillary blood-vessels only.

The further course taken by the nerves can be understood only by considering the fact hitherto unknown to all observers—namely, that the liver epithelia are separated from each other by a delicate layer of cement-substance, in the same manner as all other epithelia and endothelia. The significance of the thorns contained therein, according to the views of C. Heitzmann, is plain. The reticulum in epithelia of all kinds was first described by this observer in 1873, and it deserves mentioning that several years later E. Klein, of London, claimed to be the first to describe the reticular structure of the epithelia of the liver. Liver epithelia are in no way different from other epithelia, and the reticulum has been proved by H. Chr. Müller to be composed of living matter, while Klein does not appear to have any idea of its significance. The reticulum is connected in the center of the epithelium with the wall of the nucleus, and at the periphery with those filaments which penetrate the cement-substance, and interconnect all neighboring epithelia. A light rim of this cement-substance is always present between the endothelial wall of the capillaries and the adjacent wall of the epithelium, and again this rim is traversed by delicate grayish filaments con-

meeting the wall of the capillary with the reticulum of living matter in the epithelia. This rim of cement-substance proves to be the place where the finest fibrillæ of nerves course. In specimens treated with chloride of gold and formic acid, all structures, except the nerves, were more or less mutilated and rendered indistinct; but, in specimens previously hardened with chromic acid, washed with distilled water, and stained with a half per cent. solution of chloride of gold, the relation between epithelia and capillaries is very plain. The details can be seen only with high power (1000 to 1200 immersion) and excellent lenses. The beaded nerve-fibrillæ are connected by means of delicate threads with the wall of the capillary blood-vessels, as well as the threads in the cement-substance between epithelia. Sometimes the nerve-filament is so closely attached to the wall of the epithelium, or to the capillary, or to both of them, that the light intervening rim and the

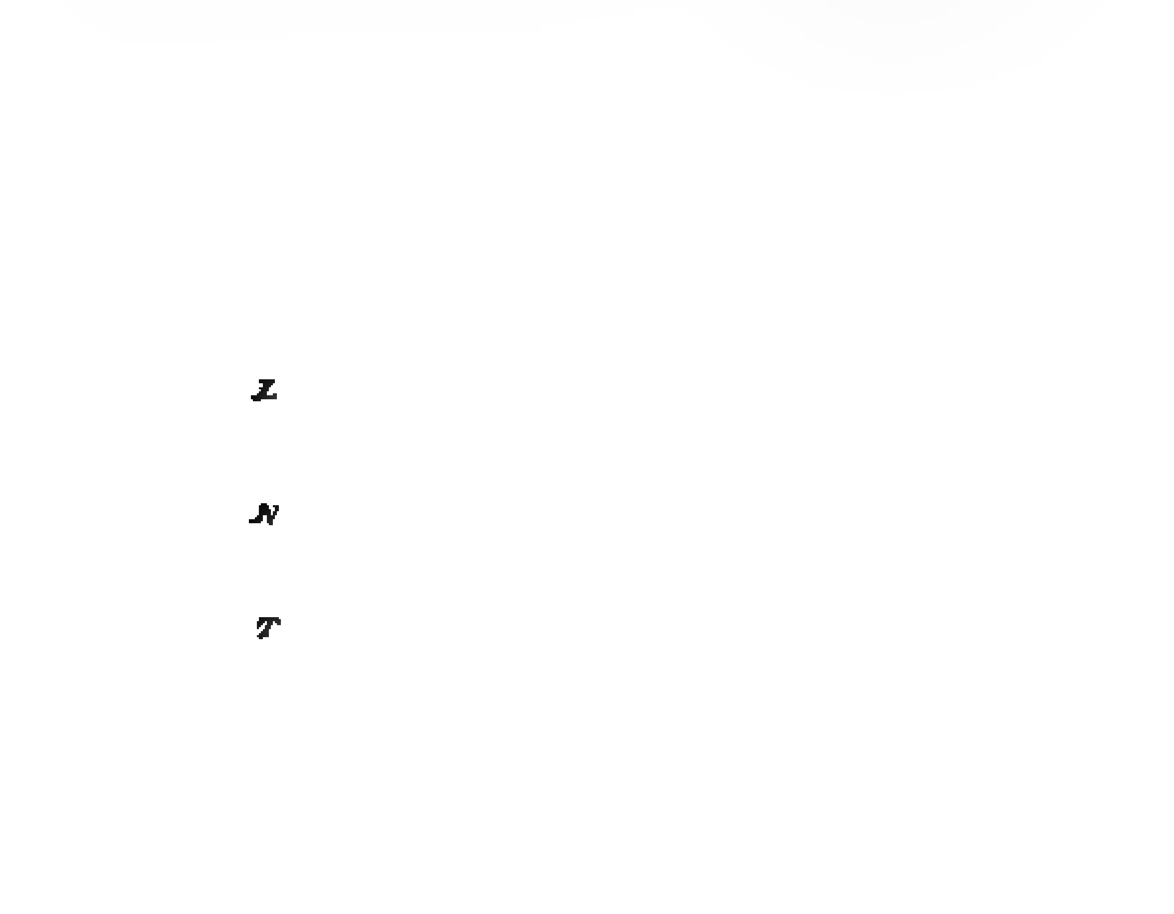


Fig. 304.—Diagram of the Terminal Nerve-Plexus of the Liver.

P, portal vein; *D*, bile-duct; *L*, capillary vessels in a longitudinal, *T*, in transverse section; *E*, liver epithelia; *B*, bundle of non-medullated nerve-fibers; *A*, axis-fibrillæ, penetrating the lobule; *N*, axis-fibrillæ in the cement-substance between epithelia.

interconnecting filaments cannot be seen. In other cases, the relations are plainly marked. (See Fig. 304.)

In the cement-substance between the epithelia I have seen delicate filaments around the capillary blood-vessels, which from analogy I think I am justified in taking for nerves. These were visible with high powers in specimens stained with carmine, but more plainly in specimens stained with

chloride of gold. In none of my large number of specimens have I ever been able to trace a nerve-filament penetrating into an epithelium, as is claimed to occur by E. Pflüger. Once or twice I observed a peculiar, pear-shaped enlargement of the nerve which seemed to be attached to an epithelium, but it was evidently only a swelled nucleus of a non-medullated nerve, without a real attachment. It often happens that a large non-medullated nerve-fiber exhibits an oblong, pear-shaped, nucleus-like formation in the axis of the fiber, whose continuity beyond the nucleus is represented by extremely delicate, beaded axis-fibrillæ.

My researches are in accordance with M. Nesterowsky's assertions that the blood-vessels of the liver, both the larger vessels of the porta and the capillaries within the lobule of the liver, are accompanied by filaments of nerves. These course in the cement-substance between the walls of the capillaries and the epithelia, and also in the cement-substance between neighboring epithelia, without ever entering the bodies of the latter. As the filaments traversing the cement-substance are formations of living matter the same as the nerve-filaments, and are in connection with the reticulum of living matter in the epithelia, we can, I think, understand how nervous impulses may be transmitted from the nerves by these bridges, the formerly so-called thorns, directly to the epithelia.

E. Pflüger* first asserted having seen medullated nerve-fibers reaching the surface of the glandular epithelia in salivary glands and in the liver. According to him, the nerves close to the epithelia lose their myeline investment, and are continued as non-medullated nerves penetrating the epithelia and terminating in the nucleus. His assertions have not been corroborated by any observer. I must deny the correctness of all his assertions concerning the termination of the nerves in the liver.

Kupfer† claims to have seen a few nerves enter the epithelia of the acinous glands along the œsophagus of the blatta (cockroach). As a re-agent he used only the vapor of ammonia.

M. Nesterowsky,‡ in his very accurate researches, has found the truth, and I concur with him in his statements, to which I have added a few more facts. This author used the fresh livers of the cat and dog, the blood-vessels of which he injected with colored glue. He used as a re-agent the chloride of gold in different degrees of dilution, and afterward placed the specimens in acetic acid for a few days, adding a drop of ammonia saturated with sulphuretted hydrogen.

Pathology. The pathology of the liver offers a wide field for research. This organ is often subject to *inflammation*, which is either *plastic* and terminates in a new formation of connective tissue,—the so-called cirrhosis,—or the inflammation is *suppurative*, resulting in the formation of abscess. Both forms have been studied in my laboratory, as shown by the following articles.

* "Nachweis der Nervenendigungen in den acinösen Drüsen und in der Leber." Archiv für Physiologie, 1871.

† "Das Verhältniss von Drüsennerven zu Drüsenzellen." Archiv für Microscop. Anatomie, Bd. ix., 1873.

‡ Ueber die Nerven der Leber. Virchow's Archiv, Bd. lxiii., 1875.

CATARRHAL OR INTERSTITIAL HEPATITIS.

BY DR. H. CHR. MÜLLER, NEW-YORK.*

The epithelia of the liver have a reticular structure common to all "protoplasmic" bodies; the granules, which are points of intersection of the reticulum, are rather coarse in the liver epithelia of man, and in that of the cat, but very fine in that of the rabbit. All epithelia are separated from each other by light rims of cement-substance, traversed by delicate, conical filaments, identical to those which connect the granules within the epithelia. The presence of these formations readily explains a number of morbid processes, for it is only the living matter forming the reticulum and the connecting threads in the cement-substance which is capable of growing, proliferating, and of producing new elements and new tissues. These new formations may, however, deviate considerably from the type of the original epithelia. The

FIG. 305.—CIRRHOSIS OF THE LIVER.

L^1, L^2, lobules of the liver, considerably decreased in size, partly blending with the interstitial connective tissue, without a marked boundary; J^1, J^2, interstitial tissue greatly augmented, holding a moderate amount of blood-vessels. Magnified 200 diameters.

bile-capillaries are excavations in the cement-substance, and are without walls of their own. In transverse section the injected bile-capillaries appear circular in the liver of the cat and oval in that of the rabbit.

In interstitial hepatitis low powers of the microscope show a considerable increase of the interlobular connective tissue at the expense of the lobules. The vascular supply of this tissue varies greatly in different parts; in some places blood-vessels are numerous, while in others so scanty that even in injected specimens large districts are almost without them. In localities

* Extracted from the author's paper, "Beiträge zur Kenntniss der interstitiellen Leberentzündung." Sitzungsber. d. Akademie d. Wissensch. in Wien, Bd. lxxiii, 1876.

where the inflammation has reached a high degree, the lobules are reduced to less than a third of their normal diameter, and, unquestionably, many of them perish altogether. The boundary between the decreased lobules and the surrounding tissue is not everywhere sharply marked, inasmuch as formations characterized by a brownish color penetrate the interstitial tissue to varying depths, indicating that a transition of one kind of tissue into the other is taking place. We also notice that the liver epithelia are no longer arranged in regular rows and tracts (this fact was known to former observers), but are now clustered in groups or separated from each other by broad interstices. (See Fig. 305.)

In order to answer the query what are the changes that have led to such a considerable wasting of the epithelia, we must examine places where there

FIG. 306.—BOUNDARY OF A LOBULE OF A CIRRHOTIC LIVER, TOWARD THE INTERSTITIAL TISSUE.

E, coalesced groups of liver epithelia, in part containing fat-globules, *M*, medullary corpuscles sprung from liver epithelia, *C*, interstitial connective tissue, with blood-vessels; *B*, cross-section of a bile-duct. Magnified 500 diameters.

is no marked boundary between the epithelia and the interstitial tissue. Here we see that in many places the cement-substance between the epithelia is missing. A number of epithelia have coalesced into groups destitute of cement-substance, or exhibiting only traces of it. Most of the granules of the epithelia are enlarged, many of them reaching the size of

nucleoli; others appear as nearly homogeneous, shining lumps of a brownish tint. In this process of growth the granules of the nuclei also participate, and, where before a nucleus was present, we often find coarse granules interconnected by filaments. Through the increased size of the granules and the coalescence of neighboring epithelia, large, coarsely granular bodies arise, in which, evidently by an outgrowth of some of the granules, new nuclei appear, never attaining, however, the size of the original nuclei. (See Fig. 306.)

In the next stage we observe marks of division appearing in the multinuclear bodies, and thus various-shaped elements arise, which remain interconnected by delicate filaments traversing the light rims. They form the

FIG. 307.—BOUNDARY OF TWO LOBULES OF A CIRRHOTIC LIVER TOWARD THE INTERSTITIAL TISSUE.

E^1, coalesced liver epithelia; E^2, multinuclear bodies, sprung from epithelia; M, medullary corpuscles, the offspring of the epithelia; J, interstitial connective tissue, holding blood-vessels; C, irregularly sinuous capillaries. Magnified 600 diameters.

indifferent, medullary, embryonal, or granulation tissue, which still retains the original brownish-yellow color of liver epithelia. As some of the corpuscles are infiltrated with basis-substance and others elongated into spindles, they produce the so-called "young or unripe" connective tissue. The interstitial tissue is, to a great extent, composed of these spindles. These formations, which with low powers of the microscope strongly resemble fibrillæ

with higher powers, are shown to be narrow, spindle-shaped elements, the arrangement of which in rows produces the fibrous appearance. At first this tissue has but little basis-substance, and the spindles exhibit a delicate granulation, owing to the presence of the reticulum of living matter. The greater the amount of firm basis-substance present, and the more nearly the connective tissue resembles cicatricial tissue, the more its striated or fibrous character becomes apparent, although in these places the primary spindle shape of the elements may still be recognized.

I have demonstrated that the transition of epithelium into connective tissue takes place, and I further maintain that the living material of the epithelia, under anomalous conditions, is capable of proliferation, and the result of this proliferation is connective tissue. (See Fig. 307.)

The relation between the liver epithelia and connective tissue in the process of cirrhosis has repeatedly been the subject of study.

C. Rokitansky * says that the reticula of the liver-cells become pale, and finally disappear in a reddish-gray or grayish mass of connective tissue. In his view the liver-cells first become cloudy, afterward shrivel and disintegrate into a detritus mixed with granules of bile-pigment, which at last disappears also.

Holm † and Hüttenbrenner ‡ maintained that in traumatic inflammation the liver may be directly converted into connective-tissue cells.

Rindfleisch § likewise assumed that, in the formation of the frame of cancer, a transformation of liver-cells into connective tissue takes place.

A. Winiwarter,‖ on the contrary, is convinced that, at least in the human liver, the epithelia are never changed into connective-tissue cells, but that the epithelia simply perish, and all the newly appearing connective tissue originates from the interlobular connective tissue of the liver.

Hüttenbrenner, by inserting a needle into the liver-tissue, has caused, around the circumference of the needle, transformation of the liver epithelia into spindle-shaped bodies. Very likely it is merely the mechanical pressure, which, in the vicinity of sarcoma or carcinoma nodules, leads to the spindle shape of epithelia. In cirrhotic livers such spindles are of not infrequent occurrence, and it is possible that they may be compressed liver epithelia; but they are never the elements of connective tissue directly arisen from the epithelia. Where such a transformation occurs, it invariably is brought about through the intermediate stage of endogenous new formation of living matter in the epithelia, and by the subsequent division of the latter. In the vicinity of shriveled lobules, in the midst of the connective tissue, we occasionally see spindle-shaped clusters of epithelia. It is quite possible that these comparatively little changed groups have escaped the process of transformation, as is indicated by their browhish-yellow color. On the other hand, the assumption is admissible that they are the remains of the endothelia of larger blood-vessels, or of the epithelia of bile-ducts. (See Fig. 308).

Fatty degeneration is of common occurrence in cirrhotic livers. We often see in an epithelial body, globules which, after being treated with strong alcohol, leave empty spaces; or sometimes, within the epithelium, small fat-

* "Lehrbuch der Pathol. Anatomie," 1861.
† "Sitzungsber. d. Wiener Akad. d. Wissensch.," 1867.
‡ "Archiv f. Mikroskop. Anatomie," Bd. v.
§ "Lehrbuch der Pathol. Gewebelehre," 1873.
‖ "Wiener Mediz. Jahrbücher," 1872.

granules are seen connected by delicate filaments with neighboring granules. In some places the fatty metamorphosis reaches high degrees, invading single epithelia, the remnants of which are found around the fat-globule. This process, however, is apparently not very common; more frequently, by coalescence of several epithelia, multinuclear bodies arise, which are in part or wholly transformed into fat, or the division of the body into irregular medullary elements has already been accomplished before the fatty metamorphosis had started. The manner in which the fatty change proceeds is as follows: Some of the coarse granules in the epithelia assume a peculiar, dull luster, and their contours become indistinct; then a number of fat-granules appear in an epithelium, but what their further changes are I am unable to tell. (See Fig. 309.)

Where several epithelia coalesce by a liquefaction of the cement-substance, it is certain also that a number of bile-capillaries perish. In other places, on the contrary, the ledges of the cement-substance are considerably widened, and we may safely conclude that a secretory activity of the epi-

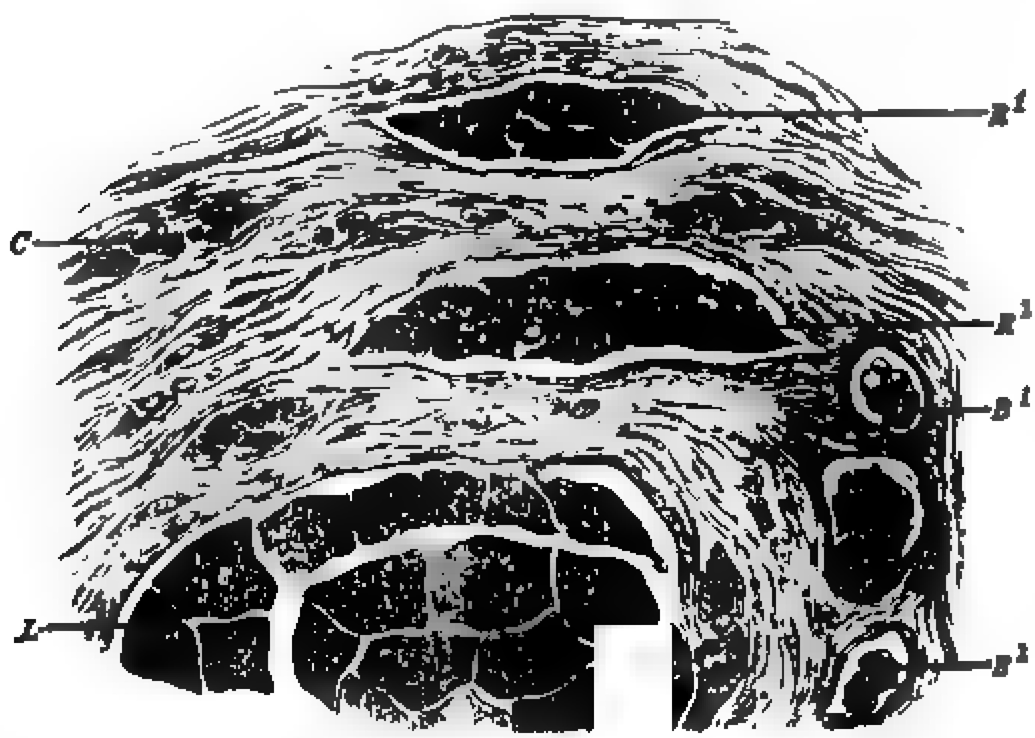


FIG. 308.—BOUNDARY OF A LOBULE OF A CIRRHOTIC LIVER TOWARD THE INTERSTITIAL TISSUE.

L, liver epithelia, R^1, R^1, spindle-shaped remnants of liver epithelia. *C*, row of medullary corpuscles, probably arisen from a former blood-vessel. B^1, B^1, bile-ducts in cross-section. Magnified 500 diameters.

thelia is possible up to the time when they are transformed into medullary corpuscles. Thus we can understand why the secretion of bile is interfered with in the highest degrees of cirrhosis only.

Larger bile-ducts are sometimes found in abundance in the interstitial connective tissue, and they may be recognized as such so long as their epithelium remains unchanged. Should this epithelium proliferate, in consequence of the endogenous outgrowth of living matter, it becomes impossible to distinguish between bile-ducts and similarly changed blood-vessels. I could never discover any new formation of bile-ducts, although it has been maintained by some authors that such a formation does occur.

A large number of the capillaries of the lobules are destroyed in the process of cirrhosis; for injected specimens plainly demonstrate that the calibers of most capillaries are considerably narrowed, and not permeable to the injected gelatine. Other capillaries, on the contrary, are irregularly widened (see Fig. 309). Thus we meet, besides capillary blood-vessels engorged with blood, solid cords, which from their course must be considered as obliterated blood-vessels.

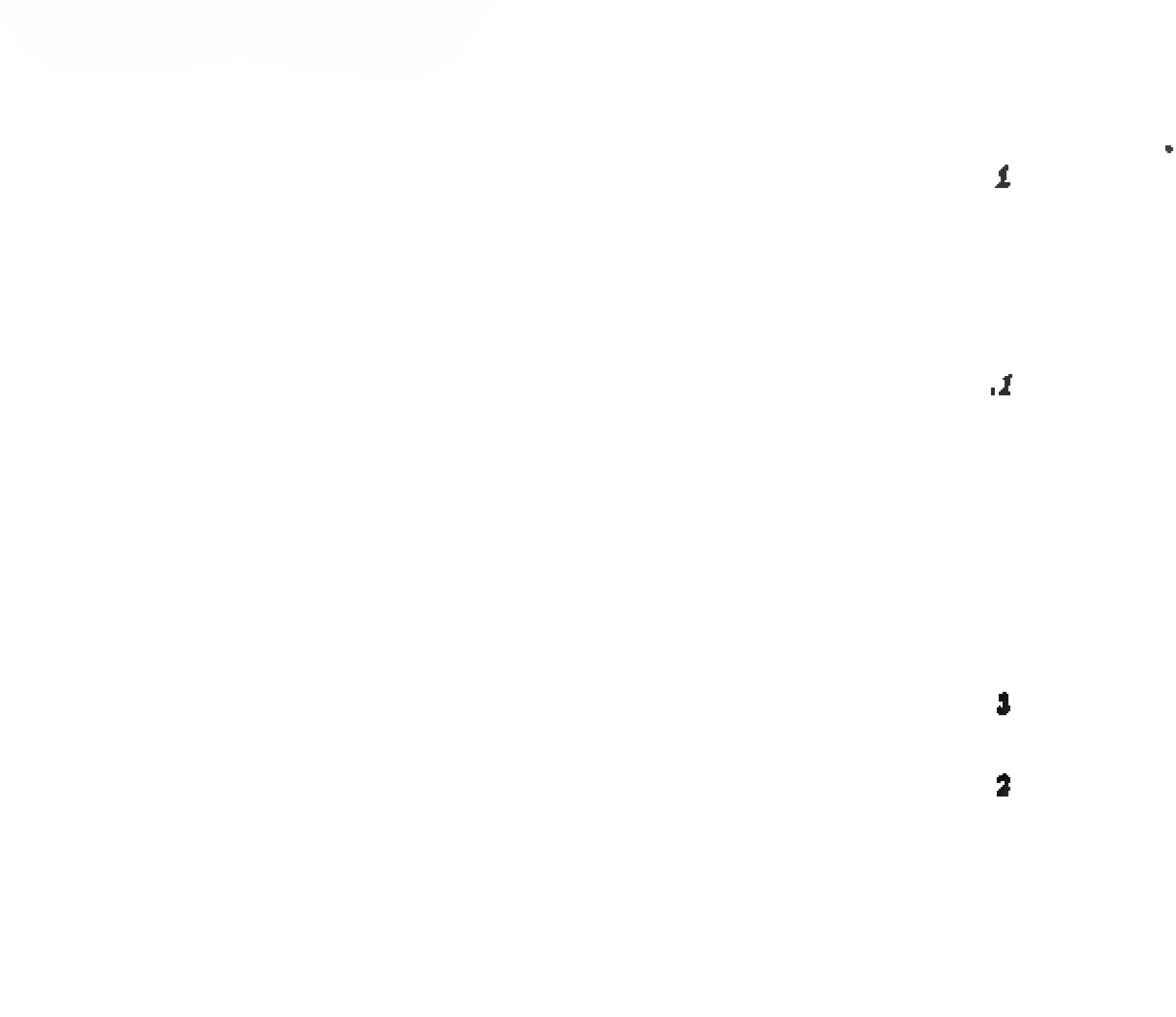


FIG. 309.—CIRRHOTIC LIVER. BLOOD-VESSELS INJECTED.

M, multinuclear bodies, sprung from liver epithelia; F^1, partial transformation of an epithelium into fat, F^2, F^3, complete transformation of epithelia into fat, C^1, C^2, irregular capillaries—injected. Magnified 500 diameters.

First, the vascular walls appear thickened and transformed into nearly homogeneous, yellowish, shining tracts, in which the boundary lines of former endothelia are no longer recognizable. This change causes a noticeable narrowing of the caliber, while later the walls fuse together into a solid cord. In such a cord a differentiation takes place into small medullary corpuscles, analogous to those arising from the liver epithelia, and producing an increase of connective tissue. In this manner numerous blood-vessels are obliterated and perish. The interstitial connective tissue in cirrhosis of the liver is known to be scantily supplied with blood-vessels.

The results of my researches are the following:

In the normal liver of man, cat, and rabbit, the glandular epithelia are

separated from each other by cement-substance, which is traversed by the spokes connecting the epithelia. The bile-capillaries are excavations in the cement-substance.

In interstitial hepatitis the living matter of the liver epithelia is augmented and the cement-substance is in part liquefied. From coalesced groups of liver epithelia multinuclear bodies arise, which, through the formation of new cement-substance, break up into a number of indifferent elements. These give rise to an abundant new formation of connective tissue.

In the process of liquefaction of the original cement-substance numbers of bile-capillaries are destroyed. The blood-vessels, through an increase of the living matter in their walls, are transformed into solid cords, which afterward divide into indifferent corpuscles, and at length give rise to fibrous connective tissue.

In *miliary tuberculosis of the liver* the inflammatory new formation invariably starts in the interstitial connective tissue. The smallest nodules discernible by the aid of the microscope are found to consist only of globular clusters of inflammatory corpuscles, in which no former constituent structures (veins, arteries, and ducts), are recognizable, and for this reason it is impossible to determine from which structure the tuberculous formation originated. Large tubercles are formed at the expense of the epithelia of the lobules, which are in this case broken down into inflammatory corpuscles in exactly the same manner as in interstitial hepatitis. The most characteristic feature of this condition is the complete destruction of the original blood-vessels and the absence of a vascular new formation. The inflammatory corpuscles are distinguished by their small size and the presence of an indistinct myxomatous reticulum similar to that found in lymph-tissue.

Syphilitic gumma originates as an inflammatory process in the interstitial connective tissue, with subsequent destruction of the liver epithelia, through their transformation into medullary corpuscles. All these corpuscles remain interconnected, representing a tissue; they give rise to a new formation of basis-substance, which is only exceptionally advanced to the stage of fibrous connective tissue, but usually remains homogeneous, and, as a rule, exhibits waxy metamorphosis. The basis-substance contains a few small plastids, generally without nuclei; and larger irregular plastids singly or in clusters, which, from their brown color, may be regarded as being liver epithelia, but slightly changed. In some places these plastids are abundantly supplied with dark brown pigment-granules, and clusters of such granules may be found scattered throughout the basis-substance. The central portions of the gumma are often disintegrated and trans-

formed into a crumbly, cheesy mass, owing to the complete absence of newly formed blood-vessels.

Microscopical Studies on Abscess of the Liver.

By J. C. Davis, M. D.*

Abscess of the liver is due in most, if not in all cases, to an inflammatory process in some of the organs of the abdominal cavity, from which the radicles of the portal system take their rise, excepting, of course, those cases which are due to a parasitic origin (Echinococcus). Abscess of the liver seems to follow only embolism in the portal vein. These embolisms are due to transported particles of pus or shreds from the wall of some pus-cavity, which, being carried into the portal system, produce either suppurative phlebitis in the *porta hepatis* — the so-called *pyle-phlebitis* — or suppurative process in any part of the liver in which an embolus may have lodged. The question why pus or tissue in suppuration, if transmitted into a healthy tissue, should again produce suppuration, cannot be satisfactorily answered. We know that pyæmia, which is invariably due to a primary suppurative process on the outer surface of the body, or in an internal organ, is very commonly accompanied by multiple abscess in the liver. The conclusion that such abscesses are mainly produced by embolism of pus gains ground, if we consider the fact that pyæmia will never ensue unless suppurative phlebitis be present in the neighborhood of the primary suppuration.

My microscopical studies are made on sections from a case of pyæmia. Sections from this liver, if viewed with a power of one to two hundred diameters, exhibit innumerable foci of inflammation. Some are yet in the earliest stage, and others in full suppuration. All inflammatory foci have their seat in the interstitial tissue, built up by the relatively small amount of connective tissue, which heretofore has been called "Glisson's capsule." Some consist merely in a slight infiltration of this tissue, others occupy its whole amount between several lobules, while others are produced by both involution of the interstitial tissue and the lobules themselves. Lastly, there are inflammatory foci in which no distinction between interstitial connective and epithelial tissue of the lobule is possible, but all look granular with a low power, which means that there have already formed, or are forming, small abscesses.

The origin of abscess of the liver is evidently the same as that of plastic interstitial hepatitis and miliary tuberculosis of the liver, although the termination is entirely different in the three kinds of inflammatory process. In the process termed plastic interstitial hepatitis, the termination consists in a new production of dense, fibrous connective tissue, the result being that which we call cirrhosis of the liver. In tuberculosis the inflammation leads to a complete loss of blood-vessels in certain territories, with the result of shrinkage of the inflammatory elements originating from all the tissues in a circumscribed territory. They become separated and isolated, thus producing that which we call a tubercle or a dry abscess.

H. Chr. Müller has demonstrated that, in cirrhosis, not only the interstitial connective tissue and the capillary blood-vessels are transformed into inflam-

*Abstract of the author's paper. *Archives of Medicine*, August, 1879. In accordance with the nomenclature adopted in this book, the term "protoplasm" is changed into "bioplasson."

separated from each other by cement-substance, which is traversed by the spokes connecting the epithelia. The bile-capillaries are excavations in the cement-substance.

In interstitial hepatitis the living matter of the liver epithelia is augmented and the cement-substance is in part liquefied. From coalesced groups of liver epithelia multinuclear bodies arise, which, through the formation of new cement-substance, break up into a number of indifferent elements. These give rise to an abundant new formation of connective tissue.

In the process of liquefaction of the original cement-substance numbers of bile-capillaries are destroyed. The blood-vessels, through an increase of the living matter in their walls, are transformed into solid cords, which afterward divide into indifferent corpuscles, and at length give rise to fibrous connective tissue.

In *miliary tuberculosis of the liver* the inflammatory new formation invariably starts in the interstitial connective tissue. The smallest nodules discernible by the aid of the microscope are found to consist only of globular clusters of inflammatory corpuscles, in which no former constituent structures (veins, arteries, and ducts), are recognizable, and for this reason it is impossible to determine from which structure the tuberculous formation originated. Large tubercles are formed at the expense of the epithelia of the lobules, which are in this case broken down into inflammatory corpuscles in exactly the same manner as in interstitial hepatitis. The most characteristic feature of this condition is the complete destruction of the original blood-vessels and the absence of a vascular new formation. The inflammatory corpuscles are distinguished by their small size and the presence of an indistinct myxomatous reticulum similar to that found in lymph-tissue.

Syphilitic gumma originates as an inflammatory process in the interstitial connective tissue, with subsequent destruction of the liver epithelia, through their transformation into medullary corpuscles. All these corpuscles remain interconnected, representing a tissue; they give rise to a new formation of basis-substance, which is only exceptionally advanced to the stage of fibrous connective tissue, but usually remains homogeneous, and, as a rule, exhibits waxy metamorphosis. The basis-substance contains a few small plastids, generally without nuclei; and larger irregular plastids singly or in clusters, which, from their brown color, may be regarded as being liver epithelia, but slightly changed. In some places these plastids are abundantly supplied with dark brown pigment-granules, and clusters of such granules may be found scattered throughout the basis-substance. The central portions of the gumma are often disintegrated and trans-

formed into a crumbly, cheesy mass, owing to the complete absence of newly formed blood-vessels.

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they were present at all, could have been by no means the main source of the pus-corpuscles.

Abscess sometimes forms in the liver, which is never made manifest by noticeable symptoms — the patient going on perhaps for years, and finally dying from some other disease, or from some traumatic cause. This never happens in multiple abscess of the liver in pyæmia, as the disease is generally rapid in its course, and death its result. In a case of formation of abscess of the liver of long standing, the abscess becomes encysted. The changes leading to the formation of a sac around the abscess have been studied by myself, in a specimen in which a liver-abscess of the size of a man's fist was formed on the convex surface, close to the peritoneum, which was found transformed into a tough pseudo-membrane of at least 4 mm. in thickness, and closely adherent to the diaphragm.

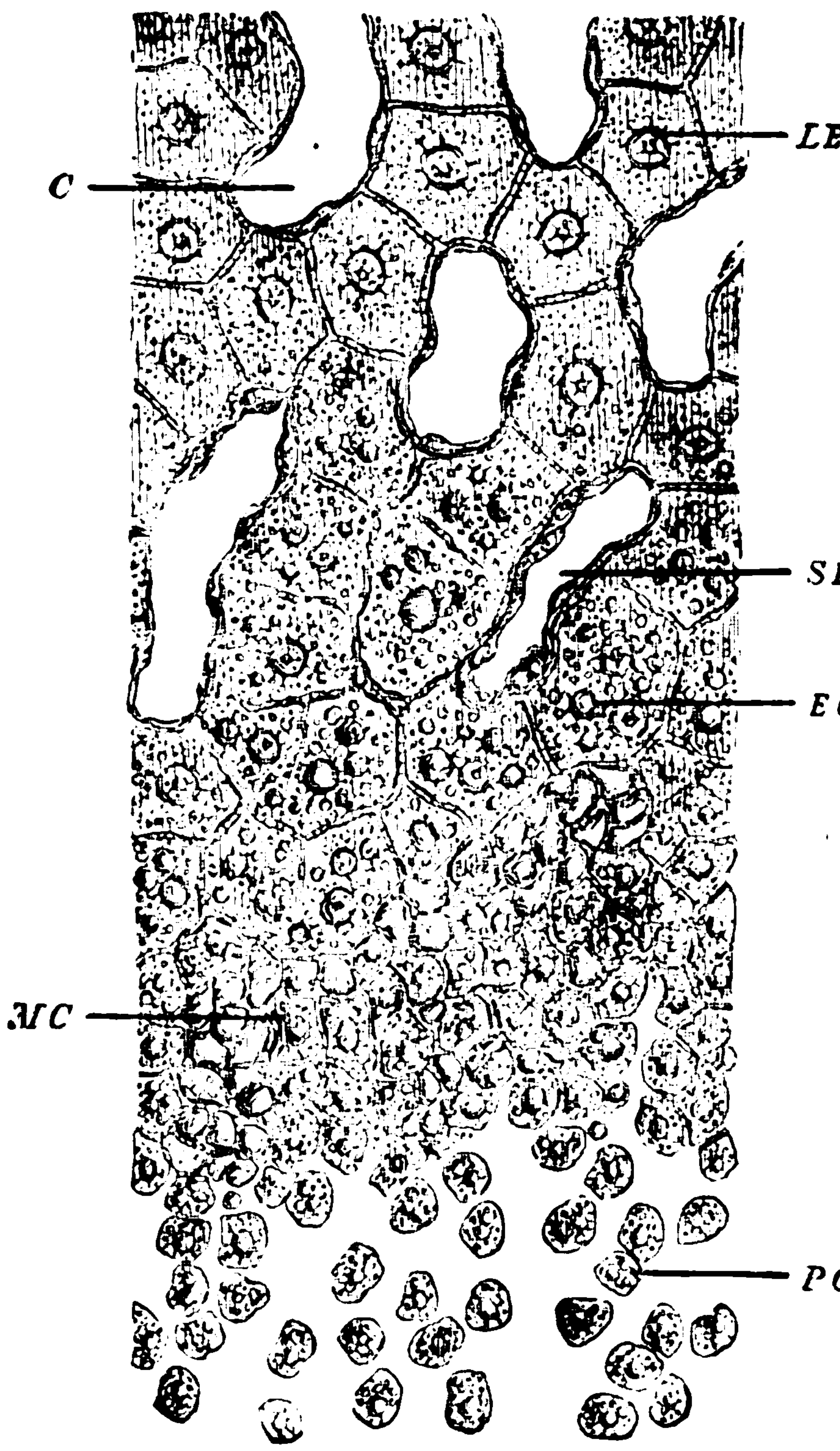

FIG. 311.—DIAGRAM OF THE FORMATION OF PUS FROM THE EPITHELIA OF A LOBULE OF THE LIVER.

LE, liver epithelia; *C*, capillary blood-vessel; *SE*, narrowed capillary, with swelled endothelia; *EG*, coarsely granular epithelia, partly transformed into multinuclear lumps; *MC*, medullary corpuscles, sprung from both the epithelia of the liver and endothelia of the capillaries, all interconnected; *PC*, pus-corpuscles.

Microscopic sections, made through the pseudo-membrane and the adjacent portions of the liver, again illustrate the way in which the pseudo-membrane, *membrana pyogena*, had been formed. It was very plain to be seen that the interstitial connective tissue of the liver and the connective tissue of the peritoneum were broken down into indifferent elements. The epithelia of the liver were transformed into medullary tissue in exactly the same way which I have described above, when speaking of the formation of an abscess. The difference was, that in the latter instance the medullary elements were left in uninterrupted continuity. In some places the medullary corpuscles became spindle-shaped, and were partly transformed into a basis-substance, that led to the formation of a delicately striated cicatricial connective tissue. The main mass of the medullary elements, however, had been simply transformed into a homogeneous or slightly granular basis-substance, with rather scanty bioplasson bodies. Inclosed in this

mass I met with scanty capillary blood-vessels, and a large number of islands of unchanged liver epithelia, which latter had escaped the transformation into medullary corpuscles and became involved in the newly formed connective tissue. (See Fig. 312.)

The conclusions I have arrived at are as follows:

1. *The inflammation invariably starts in the interstitial connective tissue of the liver, and secondarily involves a varying amount and number of the lobules of the liver.*

2. *Both the connective tissue with its blood-vessels and the epithelia of the lobules, through an increase of the living matter, become transformed into embryonal or medullary elements, thus constituting what is termed the inflammatory infiltration.*

3. *The medullary elements originally connected with each other by means of delicate thorns in turn become isolated by rupture of these thorns, and now, being suspended in a serous fluid, represent pus-corpuscles, the sum total of which is called an abscess.*

4. *The pus-corpuscles, therefore, are a direct offspring of the liver-tissue, both connective and epithelial, and no indication could be seen of an emigration of colorless blood-corpuscles.*

5. *On the boundary of the abscess the inflammatory tissue is transformed into a homogeneous or striated connective tissue, building a wall around the abscess. In the formation of this also the peritoneum shares, if the abscess has formed near it.*

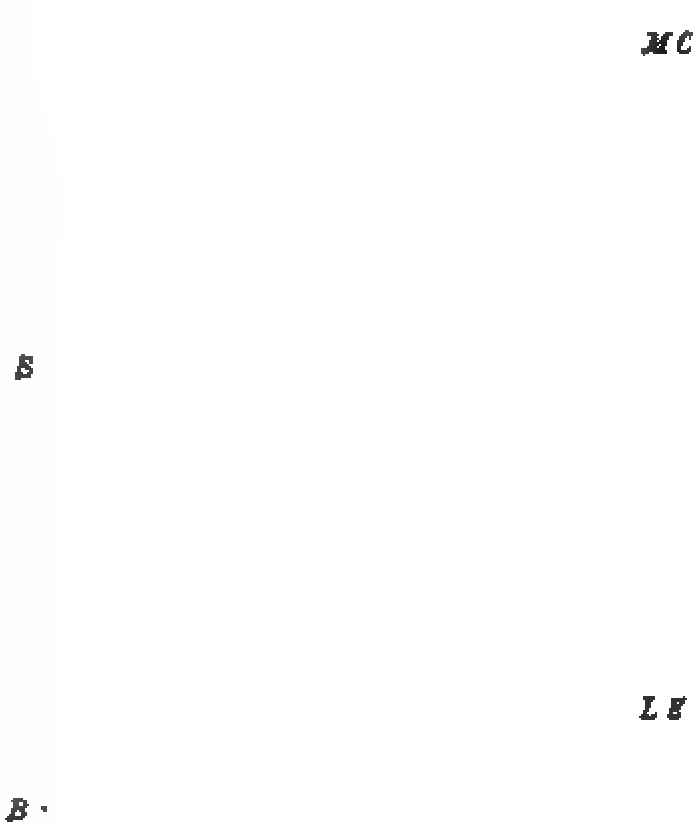

FIG. 312.—DIAGRAM OF THE FORMATION OF A CONNECTIVE-TISSUE CAPSULE AROUND AN ABSCESS OF THE LIVER.

MC, medullary corpuscles, arisen from both the epithelia of the lobule and the interstitial connective tissue. *S*, medullary corpuscles, spindle-shaped, partly transformed into basis-substance, *B*; *LE*, island of unchanged liver epithelia.

In the foregoing article reference is made to the probability of embolism of pus-corpuscles in the portal veins, causing pyæmic abscess of the liver. This is in accordance with the older views held by Cruveilhier, Piorry, Schuh, and others, while Virchow denied the possibility of such an occurrence.

In microscopic examination of the liver of a man who, after

extirpation of cancer of the throat, died of pyæmia, the first rigor having set in four days before death, infarctions and abscesses were found in the lungs, the liver, and the kidneys, nowhere large or numerous. (This is the same case to which Dr. A. W. Johnstone refers in his article, see page 546.) Sections through the tissue of this liver, at a point where an infarction the size of

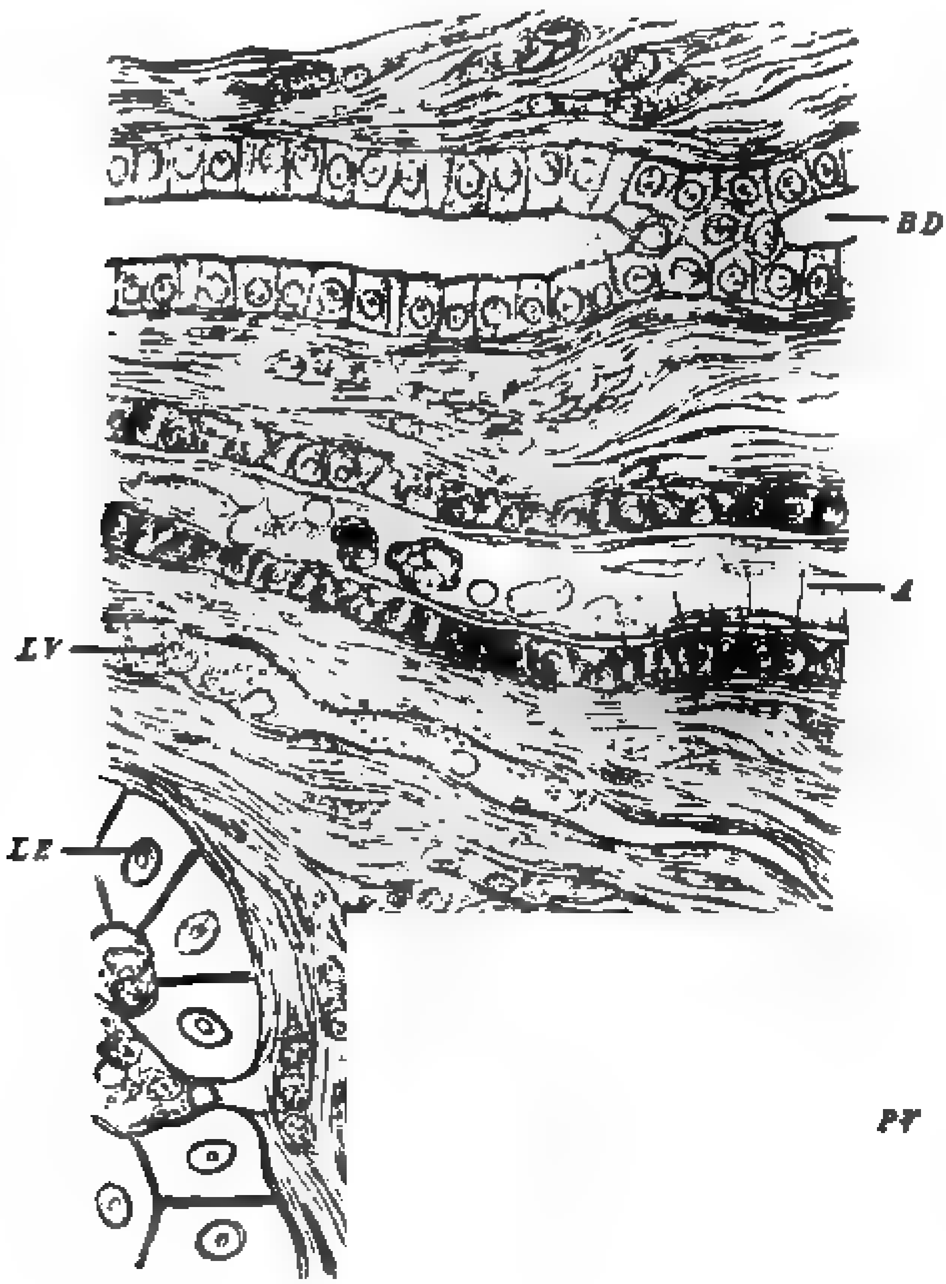

FIG. 313.—SUPPURATIVE HEPATITIS IN PYÆMIA.

PV, portal vein filled with blood- and pus-corpuscles; *A*, hepatic artery, containing blood- and pus-corpuscles, *LV*, lymph-vessel, *BD*, bile-duct, *LE*, epithelia of a lobule of the liver Magnified 600 diameters.

a hazel-nut had occurred, which, to the naked eye, looked dark purple-red at its periphery and yellowish in its center, exhibited the following peculiar features. (See Fig. 313.)

The portal veins were engorged with coarsely granular, irreg-

ularly globular corpuscles, red blood-corpuscles, and a finely granular detritus. The coarsely granular bodies were very numerous, and showed the characteristics of pus-corpuscles—viz.: the granules of living matter which they contained were of greatly varying sizes. In colorless blood-corpuscles, even of persons of a good constitution (see page 62, Fig. 20), the granules are more or less uniform in size, and their increase in such an irregular manner could be due only to inflammation. Hence, the diagnosis of pus-corpuscles in the portal veins was made. These corpuscles could not have originated *in loco*, for the surrounding connective tissue displayed very slight, if any, inflammatory changes. A branch of the hepatic artery also contained a limited number of corpuscles of this kind—on an average, smaller in size than those found in the portal veins, and pale, granular plates were also seen in the caliber of the artery, which were probably detached endothelia of the vessel itself. This specimen seems to prove that pyæmia is really caused by the embolic accumulation of pus-corpuscles, which circulate in large numbers in the whole vascular system. The older views concerning the cause of pyæmia unquestionably deserve attention, although it is difficult to explain why pus-corpuscles, collected in a certain narrow, vascular district, should excite purulent inflammation in the neighboring tissues.

At the periphery of the infarction the liver epithelia appeared unchanged, and the capillaries contained a large number of irregular, coarsely granular bodies, in some places completely choking the caliber, though without producing dilatation. All these bodies were markedly smaller than those found in the portal veins, and yet in part slightly exceeding the size of colorless blood-corpuscles. From what I have stated before, a diagnosis of pus-corpuscles in the capillaries might be admitted. Still more striking features were certain elongated bodies noticed in the calibers of the capillaries, of the size and aspect of epithelia. The possibility of their being detached vascular endothelia cannot be denied. If there were a positive proof that cancer epithelia could be carried into the circulation and produce embolisms in certain narrow, vascular districts, we would certainly be brought one step nearer to the understanding of how secondary carcinoma forms by embolism. Such a proof, however, has not yet been obtained. (See Fig. 314.).

Fatty degeneration is of rather common occurrence in the liver. We can trace the transformation of the bioplasson-granules

of the epithelia into fat granules step by step. By their coalescence fat-globules originate, which replace the central portions of the liver epithelia, including the nucleus, while, even in high degrees of fatty degeneration, every epithelium still shows a peripheral (sometimes very narrow) zone of unchanged reticular bioplasson around the central fat-globule. Further studies are required before positive statements can be made concerning the nature and cause of fatty degeneration of the liver.

Pigmentary degeneration is observed chiefly in livers of persons

FIG. 314.—SUPPURATIVE HEPATITIS IN PYÆMIA.

LE, unchanged liver epithelia. PC, capillary blood-vessels, containing blood- and pus-corpuscles. CE, epithelia (cancer-elements?) in a capillary blood-vessel. Magnified [illegible] diameters.

who had been for years affected with severe forms of so-called malarial poisoning. In such livers I have found granules of a dark brownish or black pigment, accumulated mostly in the epithelia bordering the central hepatic vein, and some coloring matter was also found, as a rule, in the neighborhood of the portal vein. Our knowledge of the causes of the formation of

pigment in the liver epithelia is very limited, although speculations on this point are numerous.

Waxy degeneration is likewise often observed in the liver-tissue, principally in persons who for years before death suffered from exhausting disease, such as syphilis, tuberculosis, nephritis, profuse suppuration, etc. The increase in the size and weight of such livers, and their lardaceous appearance, are well known; but neither the cause nor the intimate nature of the waxy metamorphosis are understood. The microscope reveals that the epithelia and the connective tissue are reduced into medullary corpuscles, or

FIG. 315.—WAXY DEGENERATION OF THE LIVER.

D, bile-duct, *C*, interstitial connective-tissue, with plastids, partly unchanged, partly waxy; *E*, liver epithelia breaking down into medullary corpuscles; *W*, liver epithelia in complete waxy metamorphosis. Magnified 500 diameters.

the epithelia transformed into clusters, with faint traces of medullary corpuscles, before the infiltration with, or the transformation into, waxy material takes place. Further studies are needed to throw more light upon the nature of this change. (See Fig. 315.)

YELLOW ATROPHY OF THE LIVER. BY J. A. ROCKWELL, NEW YORK.*

Dr. Heitzmann handed me for examination pieces from the livers of two persons, exhibiting distinct signs of yellow atrophy. One of the cases

* "Microscopical Studies in Yellow Atrophy of the Liver." *The New England Medical Gazette*, 1882.

was of an acute character, the person having died eight days after the first appearance of jaundice; while in the second case, two weeks before death, severe symptoms characteristic of yellow atrophy set in, though the clinical symptoms for some time previous had been those of interstitial hepatitis, with cirrhosis.

In specimens obtained from these two cases, a difference was noticed in accordance with the clinical history. In the first case all the evidences pointed toward a very acute destructive process in the liver, without any other complications; in the second case, the features pointed toward an acute catarrhal or interstitial hepatitis, combined with those of yellow atrophy. In fact, some observers have claimed that both these processes are so far identical that yellow atrophy must be considered merely as a very acute interstitial hepatitis. This view, however, I cannot corroborate.

Sections obtained from the first case, when brought under the microscope, exhibited as the most striking feature the want of calibers throughout the portal system, the intra-lobular capillaries, and hepatic veins. The second striking feature was the more or less marked reduction of the size of the lobules of the liver. The third point was a partial engorgement of the capillary blood-vessels of some lobules, combined with extravasation of blood. The fourth point was the disappearance of the lobules and the transformation of all the constituent tissues of the liver into a granular mass—the so-called *detritus*. In addition to these points a fifth was present in the second case, comprising the phenomena of acute interstitial hepatitis.

Whereas, in normal liver-tissues the portions between the lobules abound in large veins belonging to the portal system, in yellow atrophy such vessels are either invisible, or, if present, considerably changed in their aspect. Portal veins, which were still recognizable as such, presented an irregular, seemingly jagged, bordering line surrounding an angular, as if compressed or collapsed caliber. This, instead of containing blood, held only a brown granular mass, composed of shriveled, partly disintegrated blood-corpuscles. The branches springing from such portal veins were stretched to a narrow slit, which was bounded by medullary corpuscles, and, outside of these, by the so-called structureless layer present beneath the endothelia in the normal condition. The stretching of the vessels of the portal system to such a degree that their calibers were entirely lost, was observed in all places in which the disease had reached a high degree, though still in its initial stage. The former caliber was marked by the presence of endothelia, partly broken down into medullary corpuscles which were closely attached to each other, and on either side was seen a somewhat denser tract of connective tissue corresponding to the walls of the vein. The capillaries exhibited the same features; most of them were compressed to such a degree that the endothelia of the wall touched each other. Such thoroughly compressed capillaries were in communication with less compressed ones, filled apparently with detached endothelia and medullary corpuscles, evidently sprung from endothelia, and with scanty red blood-corpuscles.

The interstitial tissue was everywhere augmented, and composed of a large number of globular or irregular elements, such as we observe in the inflammatory process. But, while in simple acute inflammation the globular, homogeneous elements composed of solid bioplasson are largely prevailing, in yellow atrophy they were much less numerous, the finely granular bodies being largely in excess. The latter are divided into lumps of small size,

showing, with high powers of the microscope, a scanty reticulum of bioplasson in clusters, which are separated from each other by narrow, light rims, though still interconnected by delicate, grayish filaments. In most places the tracts of the former fibrous connective tissue could be recognized only by the rows of such split-up medullary corpuscles.

The bile-ducts in the interstitial tissue were well preserved, still being lined by columnar epithelium, both in longitudinal and transverse sections; but their calibers were invariably compressed. Further changes of the epithelia of the bile-duct consisted in the disappearance of the nucleus and in the division of the epithelia, partly into homogeneous, shining, partly into finely granular lumps, which, by their regular arrangement in rows, reminded one of their origin. At last, all differences between lumps sprung from connective tissue, and those arisen from bile-ducts, faded away.

The lobules of the liver were considerably reduced in size; in some places to one-half, to one-third, to one-tenth of the former diameter. This was the result of the transformation of the liver epithelia into medullary corpuscles, as is observed in inflammation generally. The gradual changes of the epithelia resulting in this destruction were as follows: First, the nucleus becomes invisible, due, as revealed by high amplifications, to its splitting up into a reticulum similar to that constructing the epithelial body. Next, the ledges of cement-substance between the epithelia disappear, and a number of epithelia coalesce into granular masses containing a varying number of granules and globules of fat. In this stage the rows of liver epithelia are still seen. With higher powers we recognize the granulation of epithelia to be due to the presence of their bioplasson reticulum, which is very much more marked than in the normal condition. This distinctness of the reticulum is due to an increase of the size of the meshes and a scanty new formation of bioplasson within the epithelia; in fact, coarse granules of bioplasson, and homogeneous, shining lumps, are found in them exceptionally only. The next step in the destruction of the epithelia is that within the cluster new lines of division appear, dividing the clusters into numerous, irregular medullary elements, all of which are composed of rarefied bioplasson reticulum, and none of which have a nucleus. (See Fig. 316.)

In some lobules, likewise decreased in size, the blood-vessels were engorged and the interstitial tissue crowded with red blood-corpuscles. The changes of the epithelia of such lobules were the same as before described. As the engorgement of the capillaries and the extravasation of blood in some places occupied quite extensive fields, I cannot help suggesting that what the authors have termed "red atrophy" of the liver, combined with "yellow atrophy," is due only to the engorgement of the blood-vessels and an extravasation of blood.

In the highest degrees of the disease the lobules of the liver had entirely disappeared, and, as a residue of the former liver-tissue, nothing was left but an accumulation of medullary corpuscles, or particles of varying sizes, between which were seen small tracts composed of spindles, besides a varying number of fat-globules. The most marked feature of this tissue was the absence of new formation of living matter. Indeed, only a few larger lumps, composed of a somewhat coarser reticulum of bioplasson, could be seen, while the main mass was an aggregation of small lumps, indistinctly bordered by light interstices, and marked by the absence of nuclei and the presence of an

extremely rarefied bioplasson reticulum. The connection of the lumps and of the reticulum itself was *nowhere broken*, so much so that this remnant of the former liver-tissue still deserves the name of tissue, and cannot be called *detritus*. Where the living matter of the constituent tissues of the liver, which is so noticeably decreased in amount, has gone to, I am unable to say. Nevertheless, I am positive that the reduction of the size of the whole liver is entirely due to a loss of its living matter.

As before mentioned in the second case which I examined, there were marked features of acute interstitial hepatitis. The interstitial tissue in some places was crowded with globular inflammatory corpuscles of a coarsely granular or homogeneous appearance, several of which were inclosed in a mesh of a delicate fibrous reticulum. At the border of the lobule the stages of transition of liver epithelia into medullary or inflammatory corpuscles

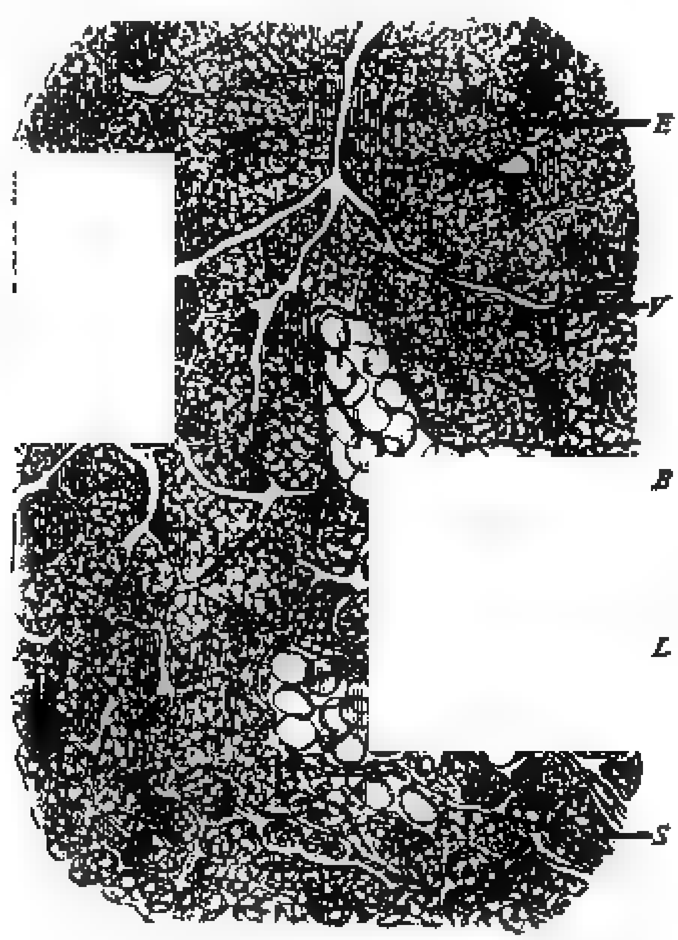

FIG. 316.—YELLOW ATROPHY OF THE LIVER.

E, cluster of liver epithelia with indistinct nuclei; *V*, compressed capillaries; *B*, capillary engorged with red blood-corpuscles; *L*, division of liver epithelia into irregular lumps, with a rarefied bioplasson reticulum and a few fat granules; *S*, accomplished disintegration into particles of varying sizes, mixed with red blood-corpuscles. Magnified 800 diameters.

could be plainly seen. In other places the breaking down of the liver epithelia proceeded nearly simultaneously from the epithelia of the lobule left, with the result that, instead of shining, homogeneous, only finely granular, irregular medullary corpuscles were seen. The process was essentially the same as in the first case, although of much less intensity, and there was also present a more decided inflammatory new formation than in the first

case. In the interstitial tissue, exhibiting marked inflammatory changes, there were observed in some places numerous bile-ducts, while in other places these were entirely absent.

The results of these researches may be summed up in the following statements:

1. *Yellow atrophy consists in the breaking down of all constituent elements of the liver into irregular lumps of medullary elements, accompanied by a considerable loss of living matter.*

2. *The disease has one feature in common with inflammation*—i. e., *the reduction of the constituent tissues into inflammatory corpuscles; but the essential feature of inflammation, namely, the new formation of living matter, is absent.*

3. *Fatty degeneration is no characteristic sign of yellow atrophy, as in both cases fat was present only in a small amount.*

4. *There are combinations of acute catarrhal or interstitial hepatitis with yellow atrophy, but in what causal relation to each other I have not determined.*

5. *Red atrophy, combined with the yellow, is very probably due merely to a partial engorgement of the capillaries and extravasation of blood.*

6. *Most of the vessels belonging to the portal system of the liver being collapsed, the conclusion is admissible that the disease is due to an impeded circulation in the larger portal vessels. The partial engorgement of the capillaries and the extravasation of blood could be explained by an impeded circulation in the hepatic artery.*

One of the most recent writers, J. Dreschfeld,* gives the following summary of the present condition of this subject, briefly stating the main points about which authors at present disagree:

"(1) As regards the icterus, many believed it to be of the hepatogenic, others believe it to be of the hematogenic kind.

"(2) While all are agreed that the chief lesion in the liver—whether acute liver atrophy be considered a general disease (as most observers believe) or primarily a local disease—consists in a fatty degeneration of the liver-cells, some writers (*e. g.*, Winiwarter, Wiener Mediz. Jahrb., 1872) think that the first change consists in an inflammatory process in the interlobular areolar tissue, which only secondarily causes fatty degeneration of the liver-cells. Again, according to Levitski and Brodowski (Virchow's Archiv, vol. lxx., p. 421), there is, prior to the cell-degeneration, a cell-proliferation in some parts of the liver-lobules, these observers having seen numerous liver-cells three to four times smaller than the normal liver-cells in those parts of the liver-parenchyma which had not yet undergone degeneration.

"(3) As to the relation of the red to the yellow atrophy, most pathologists now believe that the red atrophy is only a more advanced state of the yellow atrophy, and is found in cases which run a slow course (Zenker, Perls, etc.); while Klebs, on the other hand, believes the two to be essentially different processes.

"(4) The red atrophy is characterized by a more complete disintegration of the liver-cells, by the presence of an interlobular, embryonic tissue, and of rows of cells resembling glandular tubes, supposed by some to be proliferating biliary ducts (Cornil and Ranvier), by others to be the surviving columns of hepatic cells (Thierfelder, in Ziemssen's 'Cyclopedia,' vol. ix., p. 254).

* "On the Morbid Histology of the Liver in Acute Yellow Atrophy." *Jour. Anat. and Physiol.*, Lond., 1880-1, xv., 422-430.

"(5) Lastly, some observers (Waldeyer, Zander) have discovered bacteria in the atrophied liver. (In Zander's case, however, the autopsy was not performed until fifty-eight hours after death.)"

In 1854 and 1862 H. Lebert * gave a careful analysis of seventy-two cases, together with an abstract of the literature of acute yellow atrophy from 1660 to 1862.

This subject has since been treated at length by A. Thierfelder, † who brings down the discussion to 1877. I have examined twenty-eight contributions published since this date, which, with the exception of that of Dreschfeld, I find to consist chiefly of clinical reports.

* Virchow's Archiv, 1854, vii. 343; "Archives Générales de Méd.," 1862, i., 431.
† Ziemssen's "Cyclopedia," American edition, ix., 254.

XVIII.

THE RESPIRATORY TRACT.

THE function of the respiratory tract is the exchange of gases, mainly carbonic acid gas for oxygen, and for this purpose there is free access of the atmospheric air to the lungs by means of tubular formations. The nasal cavities must be considered as the beginning of the respiratory tract, although the oral cavity can serve for the same purpose. While all cavities and canals of the body, when at rest, are closed by folds of the mucosa, the cavities and passages engaged in the respiratory function are open either by means of the surrounding bones and cartilages such as the nasal cavities, or by cartilages alone, as the larynx, trachea, and the bronchi. The lungs themselves, where the gaseous exchange takes place in all higher developed animals, are kept in open communication with the outer world by the elastic tissue, which is present in large amount in the walls of the alveoli. The lung contains air, "residual air," from the first inspiratory movement of the newly born child, the amount being merely augmented by inspiration and lessened by expiration. In the fœtus, before birth the alveoli of the lungs are closed, and such lungs are called *atelectatic*. The same condition is produced by the choking of the alveoli by the products of inflammation, or a transformation of the lung-tissue into solid connective tissue, or by the pressure of exudate in the pleural cavity. The capillaries, like all structures of the lungs, are developed before birth, but become filled with blood only after the first inspiratory movement.

(1) The two sides of the *nasal cavity* are divided into a *respira-*

tory and an *olfactory* portion. At its beginning the wall of the nasal cavity has the same structure as the skin. It is freely supplied with hairs and sebaceous glands, and covered by a stratified epithelium. Behind the pyriform aperture the stratified epithelium is changed into columnar, ciliated epithelium, whose cilia are directed toward the choanæ. The connective tissue producing the mucous layer is abundantly supplied with acinous glands, which produce a serous secretion. Toward the upper narrowed olfactory portion of the nasal cavity the ciliated epithelia disappear and are replaced by simple columnar epithelia.

In the lateral cavities, which are in connection with the nasal cavity, the thin mucosa is covered with ciliated epithelia, but the acinous glands are very scanty. According to E. Zuckerkandl, in the upper wall of the maxillary sinus there is a tongue-shaped portion of the mucosa, richly supplied with glands; this portion is characterized to the naked eye by a pale yellow color. The mucosa of the nasal cavities has an abundant vascular supply, the veins being wide and united into a plexus. On the convex surface of the concha, more particularly at its posterior extremity, the veins produce a cavernous tissue (Henle). In the lateral cavities the blood-vessels are far less numerous.

The *olfactory portion* of the nasal cavity is, according to M. Schultze, limited to its roof to the upper turbinated bone, except the lower border, and to the upper portion of the septum narium. This portion is characterized by a yellowish color, the mucosa being broader than in the respiratory portion, and freely supplied with nerves and tubular glands, and, as a rule, also with clusters of brownish pigment.

The epithelial lining attains, in this situation, a considerable size, and, as M. Schultze discovered, is composed of columnar epithelia, between which are lodged the olfactory epithelia. The latter consist, according to him, of a fusiform, nucleated body, occupying the lower portion of the epithelial row, with polar prolongations of varying lengths. The peripheral offshoot exhibits varicose enlargements, and in many animals holds on its surface delicate cilia, which have no analogue in man. The central offshoot has the features of non-medullated nerve-fibers, and very probably is in direct union with the terminal branches of the (non-medullated) olfactory nerve. The feet of the columnar epithelia proper exhibit pencil-like ramifications, serving for their attachment to the subjacent connective tissue, and are often supplied with brown coloring matter. According to S.

Exner, there is no essential difference between the columnar and the olfactory epithelia, which exhibit forms of transition, the reticular layer at the bottom of the epithelia being destined for their indirect connection with the terminal fibers of the olfactory nerve. The tubular glands (Bowman), which occupy the whole breadth of the mucosa, are said to be lined by columnar epithelia.

(2) The *larynx* is composed of a cartilaginous frame, which serves for the attachment of the striped muscles and the mucosa through the intervening perichondrium. Most of the cartilages are hyaline, but freely intermixed with fibrous, especially in the middle portion (see page 206, Fig. 79). The epiglottis, the supra-arytenoid and cuneiform cartilages are composed of reticular cartilage, and this variety is also, as a rule, found in the processus vocales of the arytenoid cartilages. The cartilage of the epiglottis is in several places divided by fibrous tracts, containing a few blood-vessels, and in its laryngeal surface excavations are seen for the reception of large mucous glands.

The mucosa of the larynx is either uniformly composed of a loose, fibrous connective tissue, or of dense fibrous tissue near the surface (vocal bands), and loose submucous tissue in the deeper portions. Both are freely supplied with elastic fibers, which are especially developed in the mucosa of the vocal bands. In the latter situation longitudinal bundles of smooth muscle-fibers are intermixed with the connective tissue. The submucous layer contains large quantities of lymph-tissue, more abundant in children than in adults, although in the larynges of the latter we find tissue of this kind in the mucosa covering the ventricles and the ventricular folds. In addition, a varying amount of fat-globules is also observed in the submucous tissue.

The papillæ of the mucosa of the larynx are very small, and it is only at the glossal surface of the epiglottis and in the region of the arytenoid cartilage that they are more marked. Along the posterior wall of the larynx, and on the ventricular folds, the mucosa is duplicated into elevations, which are often mistaken for papillæ.

At the glossal surface of the epiglottis the epithelial cover is broad and stratified, and supplied with formations similar to gustatory buds. The stratified epithelium gradually decreases in breadth after passing over the edge and the laryngeal surface of the epiglottis. Toward the lower third of the latter it is changed into ciliated columnar epithelium, which lines the

whole inner surface of the larynx, except that, over the vocal bands, delicate stratified epithelium is seen, which is most marked in the middle portions. Here, at the boundary of the connective tissue, a narrow, so-called hyaline layer is also noticed, which is found in no other portion of the mucosa of the larynx.

The epithelial cover passes, with numerous prolongations, into the connective tissue, forming acinous glands. These appear as extended, flat layers underneath the mucosa covering the vocal bands; while they constitute more or less globular formations in other portions. The largest mucous glands are found, as a rule, at the lower portion of the laryngeal surface of the epiglottis and along the posterior wall of the larynx.

The blood-vessels in the mucosa of the larynx are expanded into several flat layers, and in some places we can distinguish three such layers, whose meshes become narrower near the surface. The largest veins are found in the mucosa covering the posterior wall. The lymphatics also produce two indistinctly marked layers, the meshes of the upper layer being narrower than those of the lower. The nerves are said to be supplied with numerous ganglionic elements.

(3) *The trachea* is a rigid, elastic tube, composed of incomplete cartilaginous rings, which, at the posterior wall, are closed by a layer of fibrous connective tissue abundantly supplied with elastic substance. The cartilage of the tracheal rings is hyaline, but in the middle portions fibrous, similar to the laryngeal cartilages; the fibrous structure being more marked in adults than in children. The mucosa is in close connection with the perichondrium, and has a nearly uniform composition of delicate, fibrous connective tissue, scantily supplied with lymph-tissue, but with an ample supply of blood-vessels, among which wide capillaries and veins are the most marked. Nearer the surface a delicate layer of smooth muscle-fibers is found, arranged usually in a circular direction. In the posterior wall, at the places where the cartilage is lacking, the circular muscles produce a broad layer, uniting the blunt ends of the cartilage, and on the peripheral portion of the posterior wall large longitudinal muscle-bundles are found. The mucosa of the trachea is destitute of papillæ, but lies in folds along the inner circumference. If these are well marked in the anterior portion, then the posterior portion, where the cartilage is absent, is without folds. The innermost layer of the connective tissue produces a delicate basement-membrane, which, however, is not invariably present in all tracheæ. (See Fig. 317.)

The lining epithelium is of the ciliated columnar variety, indistinctly stratified—the cilia being directed, as in the larynx, toward the throat. Its prolongations form racemose mucous glands, lying in flat layers close above the perichondrium, and globular formations in the posterior wall; in the latter situation they are especially large and numerous. Their ducts traverse the mucosa in an oblique direction, and are lined by columnar epithelia, which, near the opening at the surface, are supplied with cilia. Similar features can also be observed in the bronchi.

(4) *The lungs* are composed of minute *cells* or *alveoli*, which are inclosed by fibrous connective tissue, a group of alveoli being connected with a bronchiolus or alveolar duct. This union of alveoli and alveolar duct is called a lobule, the general shape of which is conical, with the base directed toward the periphery of

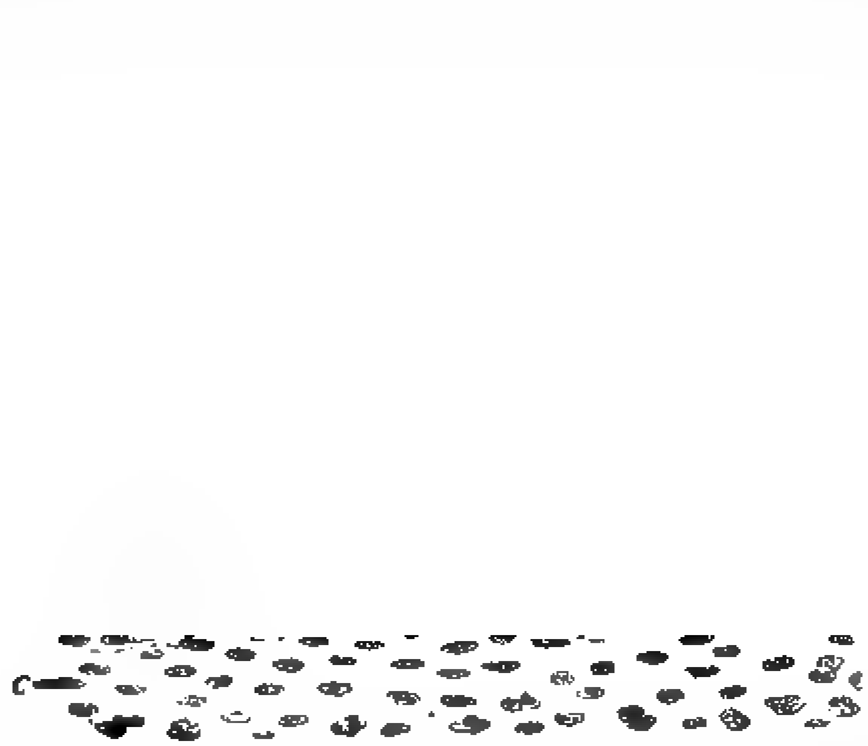

FIG. 317.—TRACHEA OF A CHILD. TRANSVERSE SECTION.

E, ciliated columnar epithelium, *S*, hyaline or basement-layer, *F*, fibrous connective tissue of the mucosa, *M*, circular bundles of smooth muscle fibers, *D*, *D*, ducts of mucous glands, in longitudinal and transverse section; *G*, racemose mucous glands, *P*, perichondrium, *C*, hyaline cartilage. Magnified 200 diameters.

the lung, and its apex connected with a bronchiolus. This relation is most marked in the peripheral portions of the lungs. The terminal alveoli bear the superfluous name "infundibulum." The widening of the bronchioli into the lung-cells is abrupt, and single cells, or cells arranged in small groups, may be seen attached to the bronchiolus before it terminates into the lobule. The lobules are separated from each other by a broader layer of

connective tissue, and the polygonal fields thus produced are distinctly marked on the surface of the lung.

The bronchi having subdivided at acute angles, the cartilaginous rings gradually disappear, and in the small bronchi are reduced to a few irregular plates. The muscle-layer, on the contrary, increases in size, and the smaller bronchi exhibit a very distinct circular layer of smooth muscle-fibers. The finest bronchi have only scanty circular muscle-fibers. The fibrous connective tissue composing the terminal bronchi is freely supplied with elastic substance, and so long as the bronchi course between the lobules they are attached to the lobules by loose connective tissue, having a capillary system of its own. The hyaline basement-layer is more marked the finer the bronchi, and is covered by a stratified columnar, ciliated epithelium. In the bronchioli of less than 1 mm. diameter, the stratification of the epithelia is nowhere marked, though they remain ciliated to the point, where the bronchiolus (alveolar duct) widens into the alveoli of the lung. The columnar epithelia gradually decrease in height, and finally blend with the flat, non-ciliated epithelia, covering the inner surface of the alveoli. All bronchi are supplied with acinous mucous glands, which are located above the muscle-layer, and become fewer and smaller as the bronchi decrease in size. In the bronchioli only simple acinous glands are found, which disappear altogether when the bronchiolus enters a lobule.

Each lobule of the lung is composed of a number of alveoli, which are semi-globular protrusions, separated from each other by folds or septa of connective tissue. The septa, together with the delicate inclosing connective tissue, constitute the wall of an alveolus. The connective tissue is marked by a rich reticulum of elastic fibers. The separating folds are never entirely effaced, even in an expanded lung; though by the inspiratory act they become more shallow, as is demonstrated by the examination of lungs, into the aërial passages of which air or gelatine had been injected before hardening in chromic acid.

The vascular supply of the lungs is very abundant. The arteries which carry the venous blood are characterized by their straight course; while the veins which carry the arterial blood have an irregular, slightly sinuous appearance. Both accompany the bronchioli, the arteries being surrounded, besides the muscle-layer, by a marked adventitial coat of fibrous connective tissue. The bronchi have an independent system of blood-

vessels, destined also for the nutrition of the adventitial coat of the larger blood-vessels; their capillaries, however, inosculate with those of the alveoli of the lung.

The branches of the pulmonary artery, upon reaching the lobules, rapidly decrease in diameter, and supply the alveoli with a rich reticulum of capillary blood-vessels, which is located directly underneath the flat, alveolar epithelium, and is often seen, toward the central space, rising above the level of the

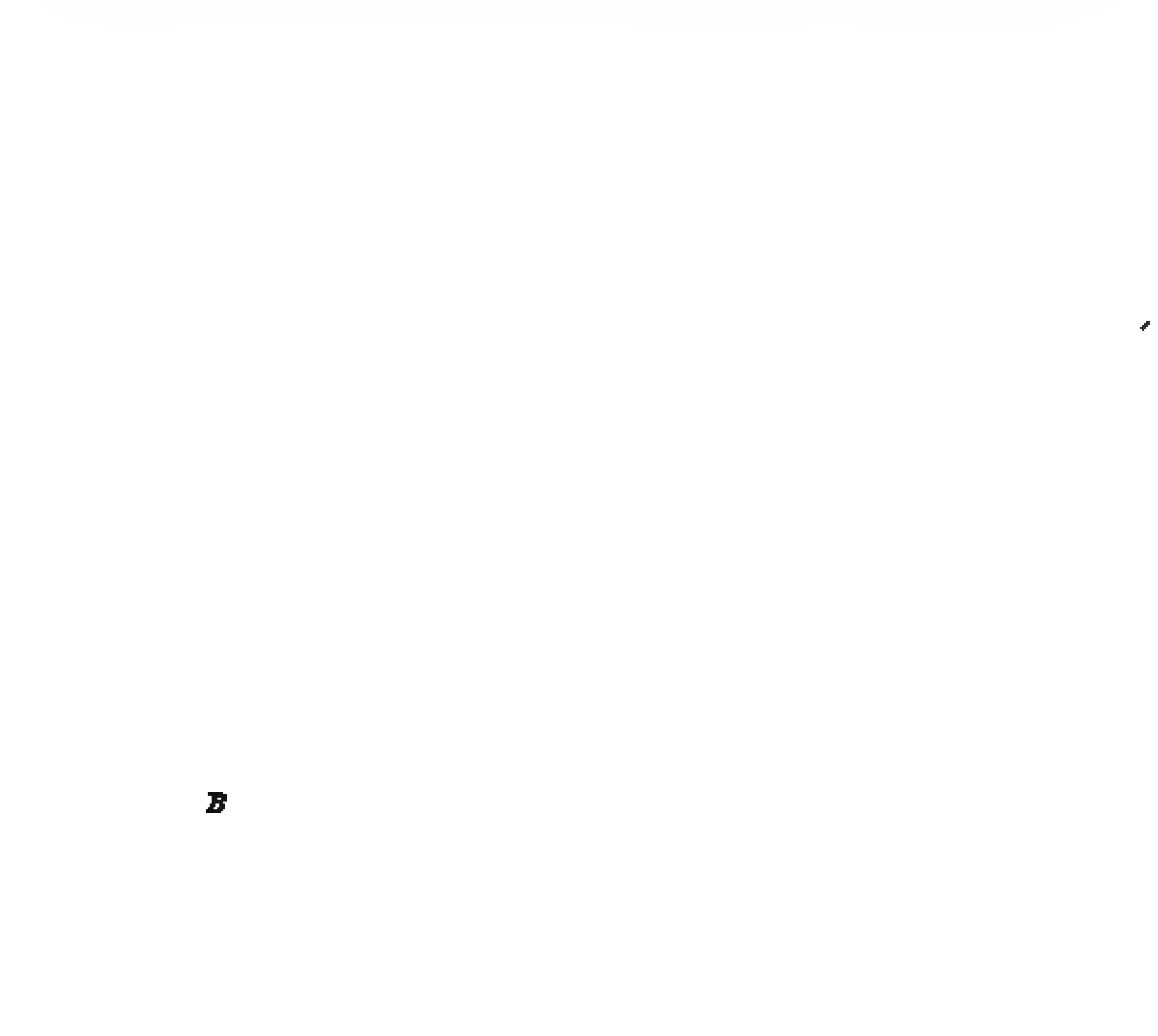

FIG. 318.—LUNG OF MAN. BLOOD-VESSELS INJECTED.

A, pulmonary artery; *C*, capillaries of the alveoli; *W*, walls of the alveoli; *B*, bronchus, in transverse section. Magnified 200 diameters.

alveolar wall. In such bulging portions the endothelia of the capillaries are easily discerned. (See Fig. 318.)

In sections made through injected and hardened lungs, the walls of the alveoli are marked by the presence of the pre-capillary, arterial, and venous vessels, and by an apparently more abundant reticulum of capillaries. Some of the alveoli exhibit the capillary reticulum in parts or throughout their

entire extent, while other alveoli appear empty. Both these conditions become intelligible if we bear in mind that the blade of the knife passes through some alveoli near their periphery, and through others across their centers; the former will show the capillaries in front view, in the latter none at all will be visible. The thickening of the capillary reticulum along the walls is due simply to their optical shortening in the top view of the septa. If we look into a basket, the bottom gives the hurdle-work in front view, therefore extended, while the walls show the hurdle condensed, and thus the wall appears thickened. By this *simile* the structure of the lung becomes easily understood.

Upon applying the high powers of the microscope, we recognize the broad capillary reticulum at the bottom of the alveoli, while the same reticulum appears shortened and condensed along the septa. Close above the blood-vessels we see the extremely delicate layer of flat epithelia, which has often the appearance of a granular mass with regularly interspersed nuclei, while the cement-substance is not plainly marked. The injection of a solution of nitrate of silver brings into distinct view the dark brown lines of the cement-substance, interrupted by delicate, transverse light lines, which correspond to the connecting filaments (thorns). F. E. Schulze discovered two varieties of lung-epithelia, viz.: small, coarsely granular, and large, pale, nearly homogeneous bodies; this difference is marked only in those human lungs which have been engaged in respiration. Henle maintains that the epithelium cannot be seen in human lungs; but there is no difficulty whatever in observing it even in injected specimens. (See Fig. 319.)

Neither lymphatics nor nerves seem to be very numerous in the lungs, and neither the origin of the former nor the termination of the latter are yet explained. Some authors assert that the lymphatics of the lungs are mere clefts in the connective tissue, without any walls of their own. As we know that the lymphatics everywhere constitute a closed system of vessels, with an endothelial lining, contrary assertions, especially regarding the lymphatics of the lungs, unless clearly demonstrated, deserve little attention. The ultimate terminations of the nerves have not yet been discovered.

Pathology. In autopsy the lungs of adults are seldom found in a perfectly normal condition. Besides the hyperæmia which accompanies fatal diseases, serous effusion, called *œdema of the lungs*, is often met with, representing a secondary and concomi-

tant condition of different diseases which terminate fatally. In microscopical examination of specimens of lungs hardened in a solution of chromic acid, œdema can be diagnosticated by an engorgement of the capillaries with blood, by a slight enlargement of the interstitial connective tissue, due to the saturation with a serous liquid, without marked inflammatory changes, and by the presence of a finely granular mass, the coagulated sero-albuminous liquid within the alveoli. In this mass are imbedded a comparatively small number of red blood-corpuscles of bioplasson bodies, which are probably emigrated colorless blood-

FIG. 319.—ALVEOLI OF THE LUNG OF MAN. BLOOD-VESSELS INJECTED.

A, alveolus; *V*, pulmonary vein, sprung from the union of the capillary reticulum; *W*, wall of the alveolus. *E*, flat epithelia, covering the inner surface of the alveolus. Magnified 500 diameters.

corpuscles, and detached epithelia of the alveoli, which are swollen and partially dropsical.

Pigmentation of the lungs is never found in newly born children, but is marked in proportion to the exposure of the individual during life to a smoky or dusty atmosphere. The lungs of tobacco-smokers and coal-workers show high degrees of black pigmentation, which gives the tissue a peculiar variegated appearance. The lungs of laborers in coal-mines, in iron foun-

deries and in brass founderies, all show differences in color. The pigment in the alveolar epithelia consists of minute black granules, and in the interlobular connective tissue it is present in clusters. The bronchial lymph-ganglia are found jet-black in persons with pigmented lungs, owing to the coloring matter carried into the lymph-tissue from without. There is no foundation, however, for the assertion that such an accumulation of pigment causes serious diseases of the lungs, although it is unquestionably a morbid condition.

Emphysema is another morbid condition of the lungs of very frequent occurrence. It consists in a mere dilatation of the alveoli,—*vesicular emphysema*,—or in a rupture of the septa and a union of a number of alveoli—*lobular emphysema*. It is caused by forced inspiration and impeded expiration due to obstructions of the air-passages, and their consequent dilatation by coughing, in chronic laryngitis and bronchitis. Emphysema is found most commonly along the anterior borders of the lungs. The over-distention of the alveoli gradually leads to a loss of the elasticity of the wall, and to a permanent dilatation of the alveoli. In higher degrees there is a rupture of the distended septa without hæmorrhage, as the blood-vessels become obliterated before the rupture takes place. Higher degrees of emphysema invariably lead to hypertrophy of the heart, interstitial hepatitis, and catarrhal or croupous nephritis, with general anasarca and fatal termination. (See Fig. 320.)

Inflammation of the lung (pneumonia) appears in two principal varieties: *croupous or fibrinous or lobar pneumonia*, and *catarrhal or lobular pneumonia*. The former involves, nearly uniformly and in a comparatively short time, large portions of the lung-tissue, whole lobes, or the entire lung; the latter is located in single lobules or in groups of lobules, and runs a more protracted course. Children under five years of age are very rarely affected with croupous pneumonia, but the catarrhal form is of frequent occurrence in early life. Under the microscope the distinguishing features are as follows: In croupous pneumonia the interstitial connective tissue is not markedly changed or increased; the alveoli are slightly distended and filled with an interlacing coagulum of fibrine, in which are entangled red blood-corpuscles, inflammatory corpuscles, and detached alveolar epithelia in varying numbers. In catarrhal pneumonia the interstitial tissue is increased and crowded with inflammatory corpuscles; the alveoli are distended by a finely granular, albuminous exudate, contain-

ing large quantities of inflammatory corpuscles and detached alveolar epithelia, which exhibit features of an endogenous new formation of pus-corpuscles. A third variety is the *plastic interstitial pneumonia*, which is confined to the interstitial connective tissue, and which leads either to *cirrhosis* or to *hypertrophy* of the lungs. A fourth variety is represented by the destructive *purulent pneumonia*, which appears either as a uniform infiltration of large portions of the lung-tissue, or in the shape of abscesses.

(a) Croupous Pneumonia. The most striking feature of this variety is the slight change in the interstitial connective tissue—

FIG. 320.—EMPHYSEMA OF THE LUNG. BLOOD-VESSELS INJECTED.

N, *N*, unchanged alveoli; *D*, *D*, dilated alveoli, *F*, *F*, ruptured alveoli; *V*, pulmonary vein. Magnified 100 diameters.

the blood-vessels are engorged with blood; nevertheless, the walls of the alveoli are only little broadened. If we consider the enormous quantity of inflammatory corpuscles present in the alveoli, the conclusion becomes admissible that the majority of the inflammatory corpuscles are emigrated, colorless blood-corpuscles. It is not probable that either the connective-tissue frame or the detached alveolar epithelia could, in so comparatively short a time, produce such quantities of exudation corpus-

cles. In the initial stages of croupous pneumonia, or in its milder forms,—the so-called *flabby hepatization*,—the pathological changes are best observed. See Fig. 321.)

Red hepatization, under the microscope, is characterized—in addition to the engorgement of the blood-vessels—by the presence of numerous red blood-corpuscles in the exudation plug, which is found to consist of a varying amount of coagulated fibrine closely attached to the wall of the alveolus. In the progress of pneumonia a great many capillaries are destroyed, for the nearer the process approaches to *gray hepatization*, the fewer are the

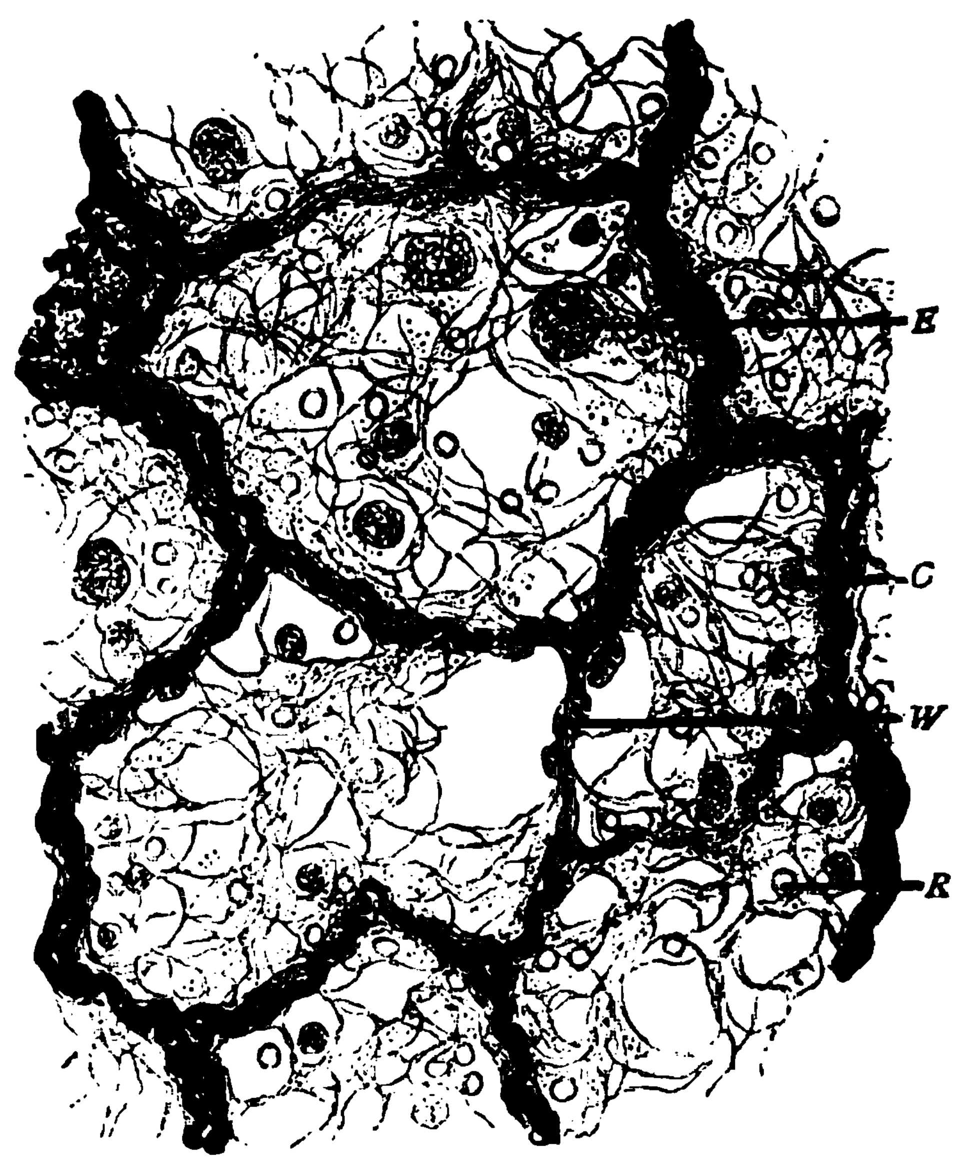

FIG. 321.—CROUPOUS PNEUMONIA. BLOOD-VESSELS INJECTED.

W, wall of alveolus; with the coagulated felt-work of fibrine filling the alveoli are entangled *R*, red blood-corpuscles; *C*, inflammatory corpuscles (emigrated, colorless blood-corpuscles?); *E*, detached epithelia of the alveoli. Magnified 500 diameters.

capillaries discernible in the alveolar walls, while those that still remain are very much distended, without being engorged by red blood-corpuscles. The gray color of the lung-tissue is largely due to this loss of capillaries. The plugs in the alveoli are found the more uniformly detached from the alveolar wall, the farther the pneumonia has advanced toward gray hepatization, and in the plugs composed of exudation-corpuscles no coagulated fibrine is discerned. With the new formation of capillary blood-vessels

and the reëstablishment of the circulation, the disease terminates in recovery, manifested by the complete throwing off of the plugs, which are saturated with liquid exudate, and thus loosened.

Sometimes in persons of a moderately good constitution, in lobar pneumonia exhibiting all features of croupous inflammation, the fibrinous exudation is scanty and the alveoli contain mainly an albuminous mass holding numbers of inflammatory corpuscles. In such cases there is sometimes no reformation of the blood-vessels destroyed in the pneumonic process, and the tissue, then deprived of nutriment, becomes firm and grayish yellow, and finally changes into a yellow, cheesy, crumbly mass. This represents the so-called *cheesy pneumonia*, which is identical with tuberculosis, although originating in larger districts of the lung-tissue and under more marked inflammatory symptoms than tuberculous foci in general. In cheesy pneumonia, the existence of which is marked by the continuance of the physical signs of pneumonia with the so-called "hectic" fever, the interstitial tissue is transformed into inflammatory corpuscles the same as in catarrhal pneumonia, and by this process in turn most of the blood-vessels are destroyed. The alveoli are filled with an inflammatory tissue which had its origin entirely in the alveolar walls. In these the elastic substance resists the inflammatory process in most, but not in all cases, and in more advanced stages of the disease numbers of inflammatory corpuscles are shriveled, owing to the want of the nourishing blood-vessels, and torn apart or disintegrated, while the elastic frame of the former alveoli is still recognizable. Shriveled inflammatory corpuscles always exhibit irregular outlines, a fine granulation, and pale nuclei, owing to a deficiency of living matter which characterizes the phthisical constitution of the patient. The combination of these appearances produces the cheesy, crumbly or tuberculous mass. A liquefaction of the mass is possible only in localities where the neighboring blood-vessels had, at least for a time, escaped the inflammatory destruction. Fatty degeneration is, as a rule, combined with the cheesy metamorphosis, as indicated by the presence of crystals of fatty acids. (See Fig. 322.)

A third and very rare termination of croupous pneumonia consists in the *brown hepatization* of a lobe. This condition is due to a new formation of interstitial connective tissue, scantily supplied with blood-vessels — *i. e.*, hypertrophy of the lung-

tissue, with profuse pigmentation of the newly formed tissue, the pigmentation being probably caused by an incomplete development of red blood-corpuscles or hæmatoblasts.

Hypostatic pneumonia is the consolidation of the pendent portions of the lung toward the end of life. It consists in an engorgement of all the blood-vessels, a sero-albuminous exudation, and a profuse detachment of the alveolar epithelia. The latter and a varying amount of red blood-corpuscles and exudation corpuscles, which in all probability are emigrated colorless blood-corpuscles, compose the plug choking the alveoli. The interstitial tissue takes no active part in the process.

(b) Catarrhal pneumonia. The most characteristic feature of this form is the inflammatory new formation in the interstitial

M

S

FIG. 322.—CHEESY PNEUMONIA, OR CHRONIC TUBERCULOSIS OF THE LUNG.

E, elastic frame of the former alveolar walls; *S*, shriveled inflammatory corpuscles and granular detritus, *M*, so-called margaric acid crystals. Magnified 500 diameters.

connective tissue. The alveoli are filled with an albuminous exudate, holding inflammatory corpuscles, produced in part by the proliferation of the connective tissue, in part by an endogenous new formation in the alveolar epithelia; to some extent they may also be due to an emigration of colorless blood-corpuscles, which occurrence is possible so long as the blood-vessels are not destroyed. With a new formation of the lost blood-vessels cure

will ensue. If, on the contrary, the inflammatory tissue-like new formation which fills the interior of the alveoli be entirely deprived of its nutrient alveolar blood-vessels, a tubercle will be the result, corresponding in size with the avascular lobular district. This is the most common termination of catarrhal pneumonia, and is almost inevitable in persons of a poor constitution. (See Fig. 323.)

So long as the inflammatory corpuscles remain interconnected by delicate filaments—*i. e.*, remain a tissue—small districts, notwithstanding the lack of blood-vessels, may become supplied with basis-substance similar to that of cartilage, the so-called horny

FIG. 323.—CATARRHAL PNEUMONIA OF A CHILD, CHANGING TO TUBERCULOSIS.

UF, unchanged wall of alveolus. *IF*, wall of alveolus crowded with inflammatory corpuscles; *C*, alveolus filled with coagulated albumen, inflammatory corpuscles, and *E*, detached alveolar epithelia; *D*, cluster of inflammatory corpuscles, in commencing shrinkage. Magnified 500 diameters.

metamorphosis or obsolescence of the tubercle. As soon, on the contrary, as the connection of the inflammatory corpuscles is broken, and the inflammatory new formation ceases to be a tissue, the corpuscles will shrivel, in part become disintegrated—in short, undergo the "cheesy" metamorphosis. In the surrounding lung-tissue, which is still provided with blood-vessels, a new formation may ensue, resulting in the production of a

fibrous capsule. Thus the cheesy focus is encysted, and may be rendered innocuous by fatty metamorphosis and subsequent calcification.

Saturation of the cheesy focus with a sero-albuminous exudate from the surrounding inflamed tissue will lead to the formation of a tuberculous cavity, the size of which will at first correspond with that of the original cheesy focus, while afterward the cavity becomes enlarged by similar inflammatory changes in the surrounding capsule itself, which result in the formation of cheesy foci, presenting all the appearances minutely described in the chapter on tuberculosis.

A complete cure of the tubercle is effected by a profuse new formation of connective tissue in its neighborhood, with the result of a dense, fibrous, cicatricial callosity. This termination of the original catarrhal pneumonia is known by the term *cirrhosis of the lung.* Large portions of lung-tissue, usually of the apices, are thus transformed into solid fibrous connective tissue, more or less pigmented, according to the amount of pigment present in the lung-tissue before the start of inflammation. In the callosity are inclosed compressed alveoli of the lung and cheesy foci in a more recent process, and calcareous nodules in an older. The latter represents, as a matter of course, a cure. The callosity is always marked by scanty vascularization. If, on the contrary, a new inflammation ensues in the callosity—subacute tuberculosis—with a complete loss of the blood-vessels in a certain portion, this will become a tubercle, and the process will, though slowly, advance to destruction of the lung-tissue. This is the reason why, in cirrhotic portions of the lungs, all stages of tuberculosis may be found, both those tending toward a cure and those tending toward ulcerative destruction. (See Fig. 324.)

Acute miliary tuberculosis is an inflammatory process, just as is chronic tuberculosis. No positive proofs have yet been furnished that miliary tubercles originate from embolism of vascular districts of the lung-tissue, although such an embolic process is highly probable. In the earliest stages of the formation of a miliary tubercle we observe all the characteristic features of catarrhal pneumonia. The smallest so-called sub-miliary tubercles are inflammatory foci, involving only a few alveoli; while larger tubercles originate from a coalescence of a number of solidified alveoli. In the early stages of the inflammatory infiltration the elastic fibers of the alveoli mark the boundaries of the alveoli,

while later even the elastic fibers are destroyed by liquefaction of their basis-substance. The most characteristic feature of this condition is the absence of blood-vessels within the tubercle. In injected specimens we observe a small number of capillaries entering the most peripheral zone of the tubercle, while around it the blood-vessels remain intact, and simply overlap the nodule. In its neighborhood emphysematous alveoli are often found. (See Fig. 325.)

With higher amplifications of the microscope we notice in the tubercle a mass of inflammatory corpuscles with an extremely delicate myxomatous reticulum. The corpuscles are character-

FIG. 324.—CIRRHOSIS OF THE LUNG, CAUSED BY SUBACUTE TUBERCULOSIS. BLOOD-VESSELS INJECTED.

A, compressed alveolus; *I*, acute inflammatory infiltration of the interstitial tissue; *F*, newly formed, fibrous (cicatricial) connective tissue; *C*, scanty blood-vessels. Magnified 500 diameters.

ized by a fine granulation—*i. e.*, they are supplied with a little living matter only. In the central portions of the tubercle multinuclear bodies are often found, the origin of which is not fully understood.

(c) Plastic interstitial pneumonia consists in the new formation of interstitial connective tissue, which leads to an enlargement of the alveolar walls, with a decrease of the number of the blood-vessels. This process is very common in insufficiencies of the valvular apparatus of the heart and stenosis of the arterial ostia,

which is followed by stagnation in the vessels of the lungs. Hypertrophy or hyperplasia of the lungs is often connected with emphysema. The new formation of connective tissue is well marked around the larger blood-vessels, both arteries and veins, more especially around the former. A rust-brown pigmentation is, as a rule, found in the augmented connective tissue, evidently due to a former extravasation of blood. (See Fig. 326.)

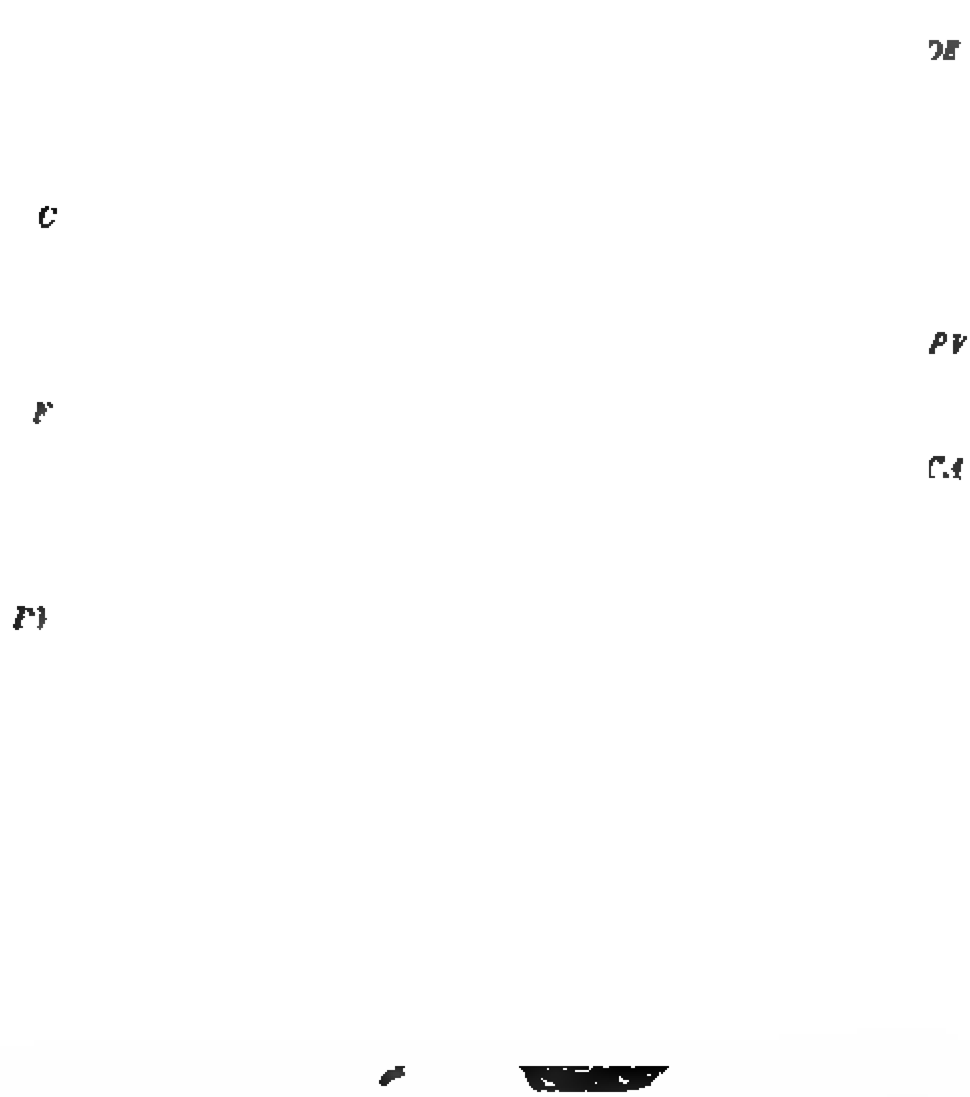

FIG. 325.—ACUTE MILIARY TUBERCULOSIS OF THE LUNG.

F, miliary tubercle; *CA*, compressed alveolus; *DE*, detached epithelia of the alveolus; *E*, emphysematous alveoli; *C*, capillaries overlapping the tubercle; *PV*, pulmonary vein. Magnified 100 diameters.

(d) Suppurative pneumonia invades either the whole or large portions of the lung-tissue in a manner similar to that of croupous pneumonia; or it appears in scattered foci, caused by embolism, in pyæmia. The distinguishing feature under the microscope

is the uniform infiltration of the interstitial connective tissue with inflammatory corpuscles, together with the plugging of the calibers of the alveoli, as in croupous pneumonia. The blood-vessels are completely destroyed, and in more advanced stages the walls of the alveoli disappear entirely. The breaking apart of the inflammatory corpuscles leads to the formation of pus. In purulent pneumonia the whole invaded portion assumes a grayish-yellow color, while in circumscribed suppuration the forming abscess is surrounded by intensely hyperæmic lung-tissue.

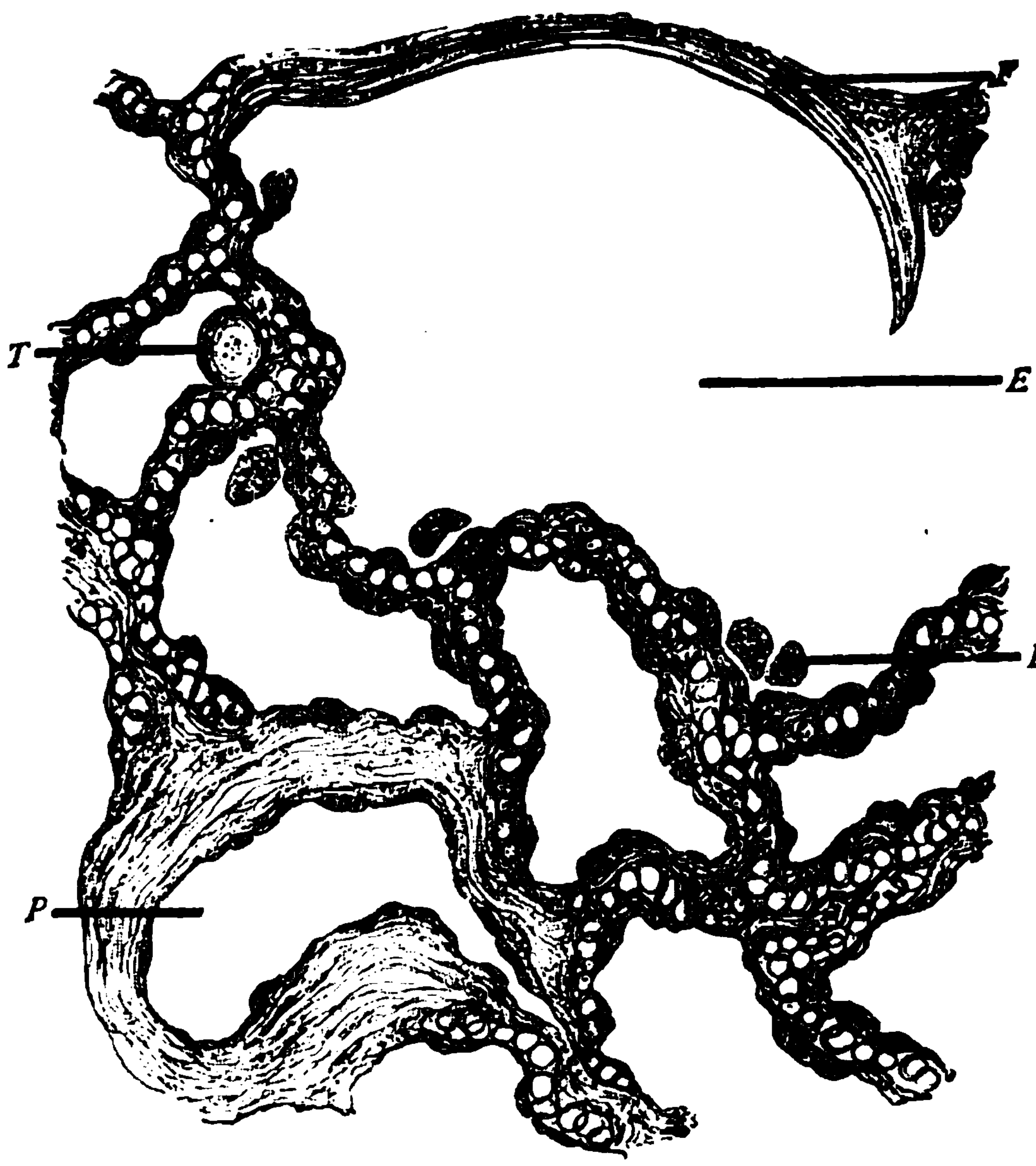

FIG. 326.—HYPERTROPHY AND EMPHYSEMA OF THE LUNG.

F, broadened frame of alveolus; *E*, emphysematous alveolus; *D*, detached alveolar epithelium; *T*, colloid corpuscle, probably sprung from alveolar epithelia; *P*, pulmonary artery, with a considerably thickened adventitial coat. Magnified 500 diameters.

SYPHILITIC HEPATITIS AND SYPHILITIC PNEUMONIA.

BY J. H. RIPLEY, M. D.*

Mrs. B., the mother of eight children — only one living, a boy of six, who has syphilitic incisor teeth — has had three successive miscarriages at the eighth month of utero-gestation. The first two of these infants were still-born; the third, the subject of my examination, lived about fifteen minutes, and even cried aloud.

The *post-mortem* examination included only the thoracic and abdominal organs, and was made in great haste. The lungs were large, of a dark grayish

* Printed from the author's manuscript.

color, firm, and only slightly crepitant on pressure, the upper lobes being the most firm. Numerous small, subpleural ecchymoses were observed scattered over the surface of both. An attempt to inflate the lungs with a blow-pipe only partially succeeded. There was no evidence of pleurisy. The heart was normal. The abdomen was large and rounded, dull on percussion over nearly its entire surface, and a large, solid body filling most of its cavity could be felt through the abdominal walls. On section this body was found to be a ponderous liver. A small area of the lower anterior surface of the right lobe had become attached to the abdominal walls by recent inflammation. About six ounces of a dark straw-colored fluid containing a few whitish flocculi were found in the abdominal cavity. The spleen was of normal size and firm. The kidneys presented nothing abnormal in gross appearance. No other organs were examined. The liver and lungs were placed in a solution of chromic acid.

Liver.—After the liver was sufficiently hardened for microscopical section, a more careful examination of its gross appearance was had. It was then observed that its great volume was largely due to the increased thickness of the right lobe. A cup-shaped depression, three-quarters of an inch in diameter, was observed on the dorsal surface of the right lobe. The cystic duct was so dilated that it formed, with the gall-bladder, a continuous pouch to its junction with the hepatic duct. The caliber of the hepatic and common ducts was also much enlarged. The liver in transverse sections exhibited numerous cysts, occupying more especially the central portions of the organ, while the periphery, to the depth of from one-quarter to one-half an inch, was comparatively normal. These cysts varied in size from a pin's head to that of a filbert, and so closely approximated one another in certain portions as to give to those parts a close resemblance to a coarse sponge. The cup-shaped depression above referred to proved to be part of a large collapsed cyst near the surface.

Under the microscope, with a power of two hundred diameters, the liver-tissue showed marked features of syphilitic hepatitis. Crowds of inflammatory corpuscles were found filling not only the inter-lobular connective tissue, but also, in many places, the interior of the lobules themselves, thus rendering the boundary line between them indistinct. With a power of six hundred diameters, the liver epithelium in many places seemed to be transformed into globular or slightly angular medullary corpuscles. Such bodies filled, also, a number of inter-epithelial capillaries, being marked in these situations by an arrangement in rows, and also by the absence of the brownish liver tint. In some epithelia containing an unusually large nucleus there were observable several concentric, circular rows of small granules. Only a few capillaries held red blood-globules. All of the inflammatory corpuscles, more particularly the concentrically granulated bodies, exhibited a peculiar luster and a homogeneous appearance characteristic of waxy degeneration. The re-agents —methyl aniline, picro-indigo, osmic acid, and iodine—yielded only negative results. This may have been due, however, to the effect on the tissues of the chromic acid solution. Cysts, too small to be seen with the unaided eye, were observable, and some of the larger ones contained bacteria. (See Fig. 327.)

Lungs. Specimens selected from the more diseased parts showed a very marked augmentation of the interalveolar connective tissue. Some of the air-cells were considerably distended by the previous inflation; others corresponded to the appearance of the normal fœtal lung, and were only recogniza-

ble by the presence of the alveolar epithelium. Those vesicles most affected by the morbid process were crowded with embryonal corpuscles and detached epithelium. In the more healthy air-cells, which had been moderately inflated, some of the epithelia had become completely detached, and some remained adherent to the alveolar wall. The epithelia, in many instances, exhibited a coarsely granular appearance, and often contained two or more nuclei, while others, again, had a nearly homogeneous, waxy-like appearance and contained several concentric, circular striations and a faintly marked nucleus. Some alveoli held, besides detached epithelia, a finely granulated, albuminous exudate, in which were imbedded a varying number of inflammatory corpuscles. Here and there was seen an alveolus, showing a delicate reticulum of coagulated fibrine. The interstitial tissue, however, presented the most marked and characteristic lesions; it was greatly increased in quantity, crowding upon and compressing the alveoli, and so filled with embryonic

FIG. 327.—SYPHILITIC HEPATITIS.

C, interstitial connective tissue, crowded with inflammatory corpuscles; *E*, liver epithelia, and *P*, capillary blood-vessels containing inflammatory corpuscles; *A*, concentrically stratified globule; *B*, remnant of a bile-duct. Magnified 600 diameters.

corpuscles as in many places to hide the underlying blood-vessels. (See Fig. 328.)

The result of the examination in this case corresponds in the main, so far as it goes, to the more extensive descriptions of these organs in syphilitic infants, given by A. Gubler.* The microscopical appearances were essentially the same as those given by Cornil and Ranvier † under the head of "Syphilitic Pneumonia and Syphilitic Hepatitis."

* Gazette Médicale de Paris, 1852. † "Pathological Histology." American edition, 1880.

The *examination of the sputa* with the microscope throws light upon a number of morbid processes in the respiratory tract. I have previously published some of the results of my researches concerning the examination of sputa.*

The corpuscular elements found in the discharges of the respiratory passages are the following: *Flat epithelia of the oral cavity; columnar epithelia from the larynx, the trachea, the bronchi, and bronchioli;* these are rarely seen ciliated, since the cilia break off easily. *Flat epithelia of the alveoli of the lungs,* which slightly surpass in diameter those of the kidneys, and, as a rule, are found swelled and globular. In smokers, or persons exposed to smoke, they contain a varying amount of pigment (charcoal) granules. In addition, *salivary, mucus-* and *pus-corpuscles* are found, besides a granular detritus, entangled with mucous threads evidently arising from the bursting or disintegration of the above-named corpuscles. *Leptothrix, micrococci,* and *bacteria* are also common occurrences in the sputa of even simple catarrhal inflammation. Lastly, the remnants of animal and vegetable food are found.

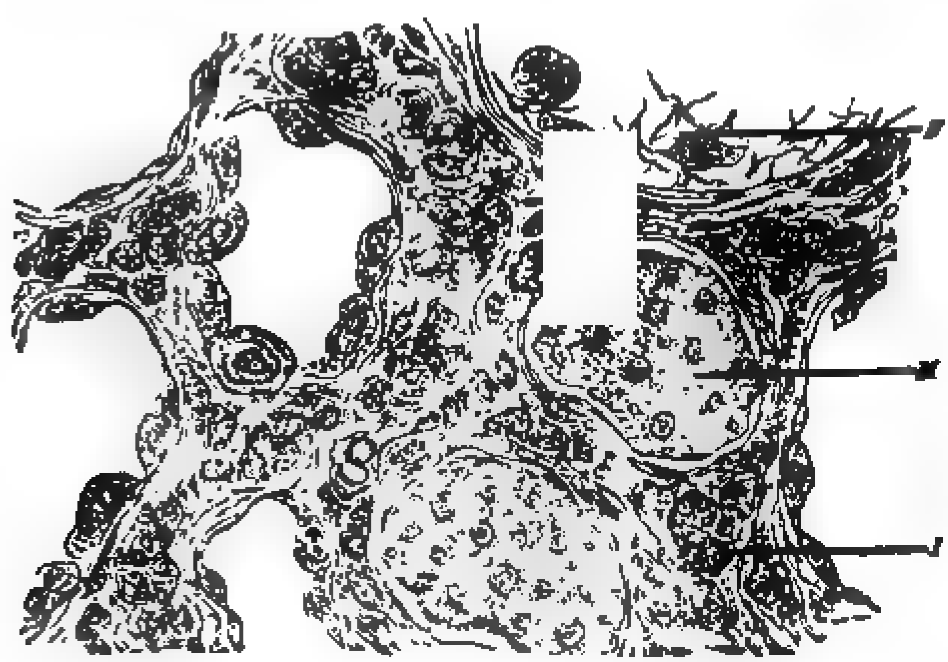

FIG. 328.—SYPHILITIC PNEUMONIA.

I, Interstitial tissue, crowded with inflammatory corpuscles; *F*, alveolus containing detached epithelia and coagulated fibrine, *M*, alveolus filled with a granular mass holding nuclei. Magnified 600 diameters.

"The most common question of physicians is: What is the difference between mucus and pus-corpuscles? The mucus, as well as the salivary corpuscles, are plastids, formerly inclosed in a shell of cement-substance, and thus forming what we call epithelia. The transformation of the contents of epithelia into saliva, mucus, and pepsin, has been carefully studied by R. Heidenhain. The transformation into mucus can be demonstrated directly on the epithelia of mucous glands of the frog's skin, and on the columnar epithelia of the small intestine of any freshly killed animal, from which we remove parts of the mucous lining with curved scissors. On the epithelia of such slices we succeed in watching the process of the formation of mucus-

* "The Aid which Medical Diagnosis Receives from Recent Discoveries in Microscopy." *Archives of Medicine*, Feb., 1879.

globules from the bioplasson of the epithelia, after we have added a drop of a very dilute solution of chromic acid or bichromate of potash, pure water being too violent in its action. We see the contents nearest to the top of the epithelia swell and become transformed into a pale, homogeneous mass. Here the shell of the cement-substance bulges out, and is thinned, until it becomes broken at the point of the greatest convexity and allows the escape of the mucus-globule. Not infrequently the whole mass of the contents is evacuated from the interior of the distended shell of cement-substance, which, being partially or totally emptied, gives the aspect of what has been termed a "cup- or goblet-cell." This lump of bioplasson is now a mucus-corpuscle, and still endowed with properties of life. Where an inflammatory process is established, the living matter of the epithelia is soon increased; in other words, their contents become coarsely granular, and, if freed in this condition, form what we call a pus-corpuscle. The main difference between a mucus- and a pus-corpuscle, therefore, is that the former looks finely, the latter coarsely granular, though both are essentially the same. Pus-corpuscles, on the average, are also more coarsely granular than colorless blood-corpuscles. The absolute identity of these bodies cannot be maintained, and the assertion of J. Cohnheim, that all pus-corpuscles — nay, all inflammatory elements, are merely emigrated colorless blood-corpuscles, is a great mistake. The formation of pus-corpuscles from epithelia and connective tissue can be directly observed, and no one has the authority to call pus-corpuscles altogether emigrated colorless blood-corpuscles, though all of us agree that these share in the formation of pus."

"We cannot tell, by watching pus-corpuscles in the sputa, from whence they come; perhaps black pigment-granules in the pus-corpuscles indicate that they have arisen from a pigmented lung. Only the presence of elastic fibers in the sputa is a sure sign of destruction of the lung, inasmuch as such fibers are present in a large amount in the walls of the alveoli. Of what nature the destruction is can be ascertained only if the elastic fibers be accompanied, besides pus-corpuscles, also by shriveled-up and broken lumps, which indicate cheesy transformation of the inflammatory product, so common in tuberculosis."

Later observations have demonstrated that, in ulceration of the larynx, the trachea, or the bronchi, elastic fibers and connective-tissue shreds may appear in the sputa, the same as in ulcerative destruction of the lung-tissue. The determination of the nature of the ulcer depends entirely upon the constitution of the patient, as diagnosed from the appearance of the pus-corpuscles. (See page 52, Fig. 20.) If the pus-corpuscles exhibit the features of the series *P*, indicative of a poor constitution, the diagnosis "*tuberculous ulceration*" is justified, regardless of the seat of the destructive process. Obviously, great care must be taken to have the oral cavity of the patient thoroughly cleansed before the sputa can be used for microscopic examination, since the shreds of connective tissue found may be the *débris* of animal food carried along by the sputa.

In one case *echinococcus of the lungs* could be diagnosed from the characteristic appearance of the echinococcus sac, emptied with the sputa.

"*Exceptionally also the new formation of myeloma in the lungs can be diagnosed by the examination of the sputa alone*, as illustrated by the following case, which occurred three years ago. A justice of this city, about sixty years of age, had a tumor in his right groin, which, after repeated extirpations, always

recurred, and recently began to grow rapidly. The consulting surgeons made the diagnosis "cancer," and foretold an approaching ulceration for which the relatives had to be prepared. The attending physician, Dr. Schöney, soon afterward brought some sputa of the patient to my laboratory, being struck by their large quantity. On microscopic examination, besides pus-corpuscles, numerous globular elements were also seen, characteristic of the so-called round-cell sarcoma or globo-myeloma. The diagnosis was: secondary formation of myeloma in the lungs, due to a primary myeloma in the groin, which latter would not ulcerate. The post-mortem examination a few weeks afterward fully corroborated my diagnosis, though I never had seen the patient. The lungs were crowded with white nodules of myeloma, and the tumor in the groin proved to be an alveolar myeloma which had never come to ulceration."

XIX.

THE URINARY TRACT.

THE essential parts of the urinary tract are those portions of the kidneys which secrete the urine, while all other membranous tubules and sacs connected with them—*i. e.*, the pelves, the ureters, the bladder, and the urethra—are merely a collecting and conducting apparatus. The investigations of R. Heidenhain have corroborated the views of Bowman that, from the capillary blood-vessels of the tuft, which carry arterial blood, only a watery liquid, destitute of salts, is exuding into the capsular space, while the saline constituents of the urine are the excretory product of those uriniferous tubules which are richly supplied with capillary blood-vessels, and whose epithelia are closely connected with the walls of the vessels. The inspissated blood contained in these vessels reabsorbs a portion of the liquid from the tubule and supplies the liquid in the tubules with a certain amount of its salts. Obviously, the whole process is accomplished through the agency of the living epithelia, and is not to be considered as a simple process of osmosis. The differences in the structure of the epithelia in certain portions of the uriniferous tubules, and the striking differences in the distribution of the blood-vessels, strongly point toward a difference in the function of portions of the tubules; but no exact demonstration of these functions, concerning the constituent elements of urine, has as yet been furnished. The Greek denomination, "dialysis," serves to conceal our lack of knowledge of the process concerned in urinary excretion in about the same manner that the word "catalysis" disguises our ignorance of the process of digestion

in the stomach. Many an eminent observer has contributed to our stock of knowledge regarding the minute anatomy of the kidneys, while the physiology of the excretion of urine is still unexplained.

(1) *The Kidneys.* The kidney consists of a cortical and a pyramidal portion, and in man is made up of from six to twelve united parts, each of which has a cortical and a pyramidal substance. The boundary between the two main divisions is irregular, and in parts illy defined; each subdivision terminates at the concave border in the center of the organ in the so-called papilla, which is surrounded by a membranous sac — the calyx. The loose connective tissue between the pyramids carries the larger blood- and lymph-vessels and the principal nerves. The surface of the kidney of the adult is smooth, being ensheathed by a dense, fibrous connective-tissue capsule; while the fœtal kidney exhibits a distinctly lobate surface, indicative of its general construction of lobes or segments. The main constituents of the kidney are the blood-vessels and the uriniferous tubules, which are held together by a delicate, fibrous connective tissue, rich in elastic substance, giving the whole structure a high degree of consistency. From the arrangement of the tubules the kidney is classified among the compound tubular glands.

The *renal artery* enters the organ in two main branches (Hyrtl), each of which, by a number of bifurcations dividing into smaller ramules, supplies an independent half. These vessels, upon reaching the boundary zone between the cortical and pyramidal substance, deviate in an oblique direction, and produce the so-called arterial bows or arches, the convexities of which, if marked at all, look toward the cortical substance. Each artery in this situation is accompanied by a vein, the veins being connected by lateral branches, and producing a sort of a venous plexus.

From the arches arise at short intervals straight arterial branches, which penetrate the cortical substance in a straight direction and divide at very acute angles; these arteries produce transverse ramules, the afferent vessels which go to form the tuft. A successful injection of the blood-vessels of the human kidney is quite exceptional, while the dog's kidney, which can be had in a perfectly fresh condition, allows a plain demonstration of the vascular supply. As the relations in the latter are very similar to those of human kidneys, they may with preference be used for demonstration. (See Fig. 329.)

The afferent vessel is either a terminal branch of the renal artery or a lateral offshoot of such a branch, which is given off without any regularity. Not infrequently the afferent vessel assumes a backward course, especially near the region lying between cortex and pyramid, in human as well as in dogs' kidneys. The ultimate terminations of the arteries and their tufts never reach the outermost portion of the cortical substance, which is supplied with capillaries only.

The afferent artery invariably exhibits a distinct middle or muscle coat, and splits abruptly into a number of capillaries, which contain arterial blood, and, by being convoluted and turned upon themselves, produce the tuft. According to C. Ludwig the formation of the tuft is easily understood by assuming that the arterial bed of the afferent vessel is abruptly widened and at the same time split into a number of very narrow (capillary) canals, which again unite into the efferent vessel: bring the surface of the opposite parts together, so that the afferent and efferent vessels are in proximity, and the tuft is complete. The formation can be readily demonstrated with a handkerchief, the two compressed ends of which are held in the two hands, one representing the afferent, the other the efferent vessel,

FIG. 329.—CORTICAL SUBSTANCE OF THE KIDNEY OF A DOG. BLOOD-VESSELS INJECTED.

Ca, capsule. *O*, outer zone, devoid of tufts. *T*, tuft. *A*, afferent vessel. *E*, efferent vessel. *R*, branch of renal artery. *Co*, zone of convoluted tubules; *S*, zone of straight tubules (medullary ray). Magnified 100 diameters.

and the whole being turned upon itself, the two hands joining, while the middle, broad portion, spread and folded, represents the tuft. (See Fig. 330.)

The *tufts*, or glomeruli, or Malpighian corpuscles, are globular formations of 0.02 to 0.03 mm. diameter, composed of a number of convolutions of capillary blood-vessels, which both in the human and in the dog's kidney are arranged in two main lobes; hence, the glomerulus is a bilobate formation of capillaries. One lobule is always larger than the other, and the summit of the larger lobule is directed toward the opening of the uriniferous tubule. Each tuft is enveloped in a delicate connective-tissue capsule (Bowman, H. Müller) in a manner similar to that in which the pericardium surrounds the heart. Both layers, the free or parietal, as well as the reduplicated glomerular, are composed of connective tissue rich in elastic substance, the glomerular portion being more delicate than the parietal; both are covered with a flat epithelial layer. The glomerular portion sends prolongations between the capillaries of the tuft, and a marked prolongation, together with the covering epithelium, into the groove between the two lobules of the tuft (Axel Key). The epithelium covering the glomerular portion of the capsule is cuboidal in the fœtus and in children, and becomes flattened in the adult; while the epithelium of the parietal portion of the capsule is always flat and blends with the cuboidal epithelium of the uriniferous tubule, the beginning of which it represents. At the point where the afferent vessel enters and the efferent leaves the tuft, the capsule turns over to the tuft, and the connective tissue at this point is more freely supplied with plastids having the appearance of nuclei than elsewhere. (See Fig. 331.)

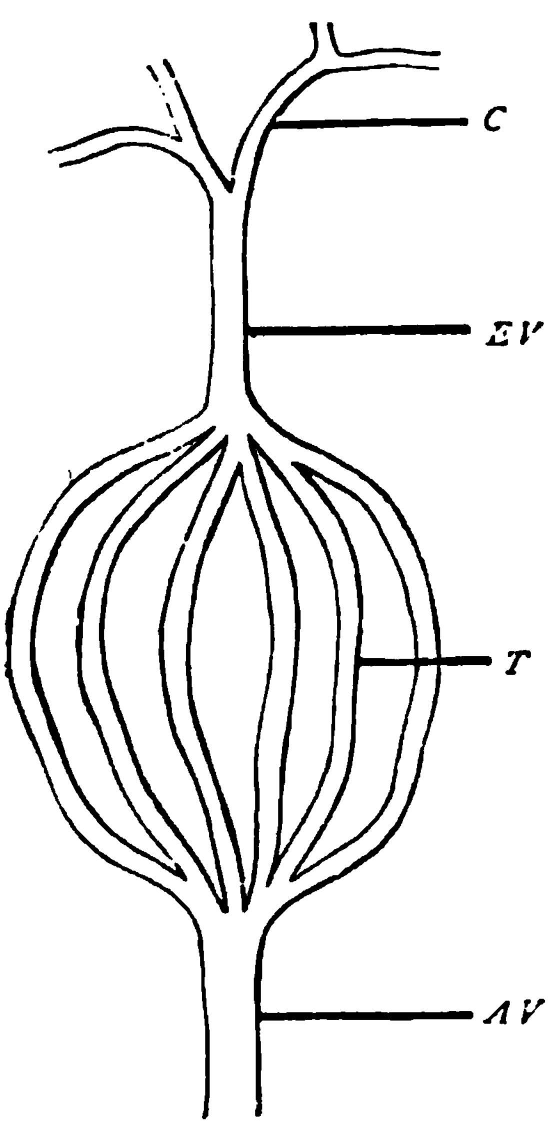

FIG. 330.—DIAGRAM OF THE TUFT (C. LUDWIG).

AV, afferent vessel; *T*, capillaries composing the tuft; *EV*, efferent vessel; *C*, capillaries for the supply of the cortical substance.

The *efferent vessel* invariably leaves the tuft near the entrance of the afferent vessel; it contains arterial blood, though the muscle-coat is very imperfect, or absent. Its diameter is decidedly

smaller than that of the afferent vessel. Soon after having left the tuft, it divides freely into capillaries for the supply of the cortical as well as the pyramidal substance. So extensive is this division that the kidney-tissue proper has no other capillaries than those derived from the efferent vessels, the pyramidal substance being, besides, supplied with capillaries from a few independent arterioles. The capillary meshes are circular in the region of the convoluted tubules, and elongated squares in that of the straight tubules. (See Fig. 329.)

The arterial arches send a few small arterial branches downward into the pyramidal substance. The main supply of this portion, however, is capillary, and of two kinds: First, the few elongated, square meshes around the straight collecting tubules; and second, the bundles of very wide capillaries, accompanying the narrow tubules. The latter are the so-called *vasa recta* of the pyramidal substance. Some authors claim that they are arteries produced directly from the arterial arches, which, however, is not correct. Others maintain that the vasa recta arise immediately from the efferent vessels of the tufts nearest the pyramidal substance (C. Ludwig); again, others consider the vasa recta as veins which originate from the capillaries of the cortical substance, in a manner similar to the portal system of the liver (Huschke, Hyrtl, Henle). We overcome all difficulties concerning the origin of the vasa recta by considering them as considerably widened capillary blood-vessels, which are prolongations of the narrow capillaries of the cortical substance—a fact which is easily demonstrated in the injected kidney of the dog. (See Fig. 332.)

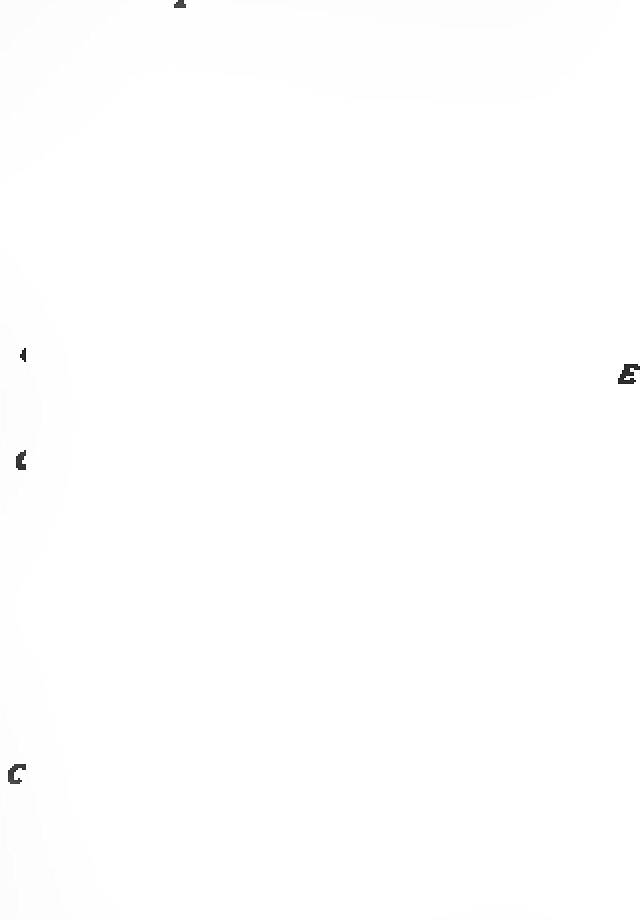

FIG. 331.—TUFT FROM THE KIDNEY OF A DOG. INJECTED.

T, capillary loops of the tuft, in connection with the afferent artery, covered by *E*, flat epithelia. *Ca*, capsule, covered with flat epithelia, in communication with *Co*, the convoluted tubule, *CL*, convoluted tubule in longitudinal section, *CT*, convoluted tubule in transverse section. Magnified 350 diameters.

The ascending branches of the arterial arches which give rise to the afferent vessels are, by most authors, termed inter-lobular arteries. This name should be abandoned, for the reason that they occupy the center of a cortical lobule (Ludwig's labyrinth). The capillaries of the cortical substance are usually considered to be of two kinds—those rising directly from the efferent vessels, for the supply of the medullary rays, and those of the labyrinth, which are prolongations of the former. This conception is, however, misleading, inasmuch as the efferent vessels produce the capillaries of the labyrinth and the medullary rays, both directly and indirectly, and there is no necessity for speaking of arterial and venous capillaries. Fig. 329 shows the distribution of the capillaries from the efferent vessels, some running first to the labyrinth, others first to the medullary rays.

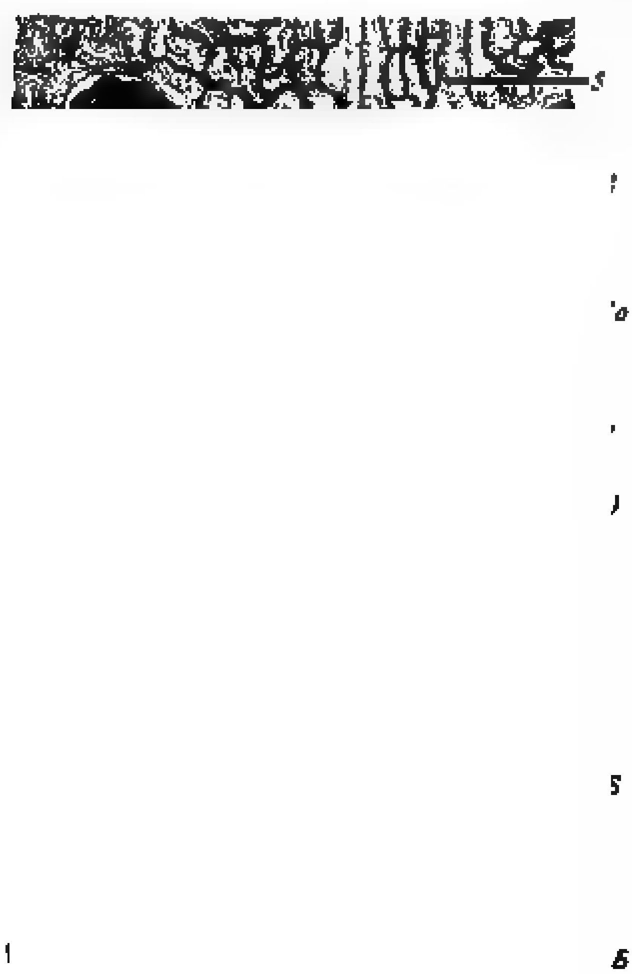

FIG. 332.—BOUNDARY ZONE BETWEEN THE CORTICAL AND PYRAMIDAL SUBSTANCE OF THE KIDNEY OF A DOG. BLOOD-VESSELS INJECTED.

A, branch of renal artery. *Co*, prolongation of the cortical substance, *T*, tuft. *S*, bundle of straight tubules. *O*, origin of the vasa recta from the capillaries of the cortical substance. *B*, bundle of vasa recta. Magnified 100 diameters.

The *veins* arise from the capillaries of the cortical substance, especially those of the labyrinth, and their confluence is often marked on the surface of the kidney in the form of stars (stellulæ Verheyenii). As the medullary rays are lost near the surface of the kidney, and the outermost portion of the cortex has no tufts, obviously the veins arise from the capillary system surrounding the convoluted tubules. The veins accompany the arteries, and empty into the venous plexus at the boundary zone between the cortex and the pyramis. The latter furnishes veins derived both from

the capillaries of the collecting tubules and from the vasa recta, the ascending loops of which empty directly into the inter-zonal venous plexus.

According to C. Ludwig, the capillaries of the capsule and of the surrounding fat-tissue of the kidney, which arise partly from small branches of the renal artery before it reaches the bounding zone, are united directly to the capillaries of the kidney-tissue.

The *uriniferous tubules* originate from the capsules of the tufts, opposite the site of the blood-vessels, as first discovered by Bowman, and terminate, after uniting and being considerably reduced in numbers, at the papilla of the pyramid. They are chiefly of two kinds: *convoluted and straight.* The former consist of convoluted tubes of the first and second order; the latter are the straight, narrow and straight, collecting tubules. The *convoluted tubules* of the first order occupy the portion around the ascending branches of the renal artery, and their sum total is termed the "labyrinth" by C. Ludwig; the convoluted tubules of the second order fill the most external portion of the cortex, in which there are no tufts. The *straight tubules*, both narrow and collecting, produce the medullary rays between the labyrinths in the cortex; while in the pyramids they run in separate bundles according to the following arrangement: First, the narrow tubules, together with the vasa recta, in the imaginary prolongations of the labyrinth, and then the collecting tubules as direct prolongations of the medullary rays of the cortex. Fig. 333 represents the generally adopted schema of the course of the uriniferous tubules, first issued by Ludwig and Schweigger-Seidel. The results were obtained both by isolation of the uriniferous tubules, by means of maceration in dilute acids, and by the study of kidneys in which the blood-vessels and uriniferous tubules had been injected with colored gelatine. In this department C. Ludwig was most successful. (See Fig. 333.)

The details are as follows: The *convoluted tubule* (of the first order) originates from the capsule of the tuft as a slightly narrowed, funnel-shaped neck, and, after repeated convolutions within the labyrinth, tends toward the medullary ray. Here it becomes (to varying depths) *narrow*, often exhibiting spiral windings (Schachowa) before decreasing in caliber, and represents the *descending branch* of the loop, or Henle's tubule. This enters the pyramidal substance, producing a distinct, angular divergence at the dividing zone between cortex and pyramid, in order to reach the bundles of the vasa recta. After reaching

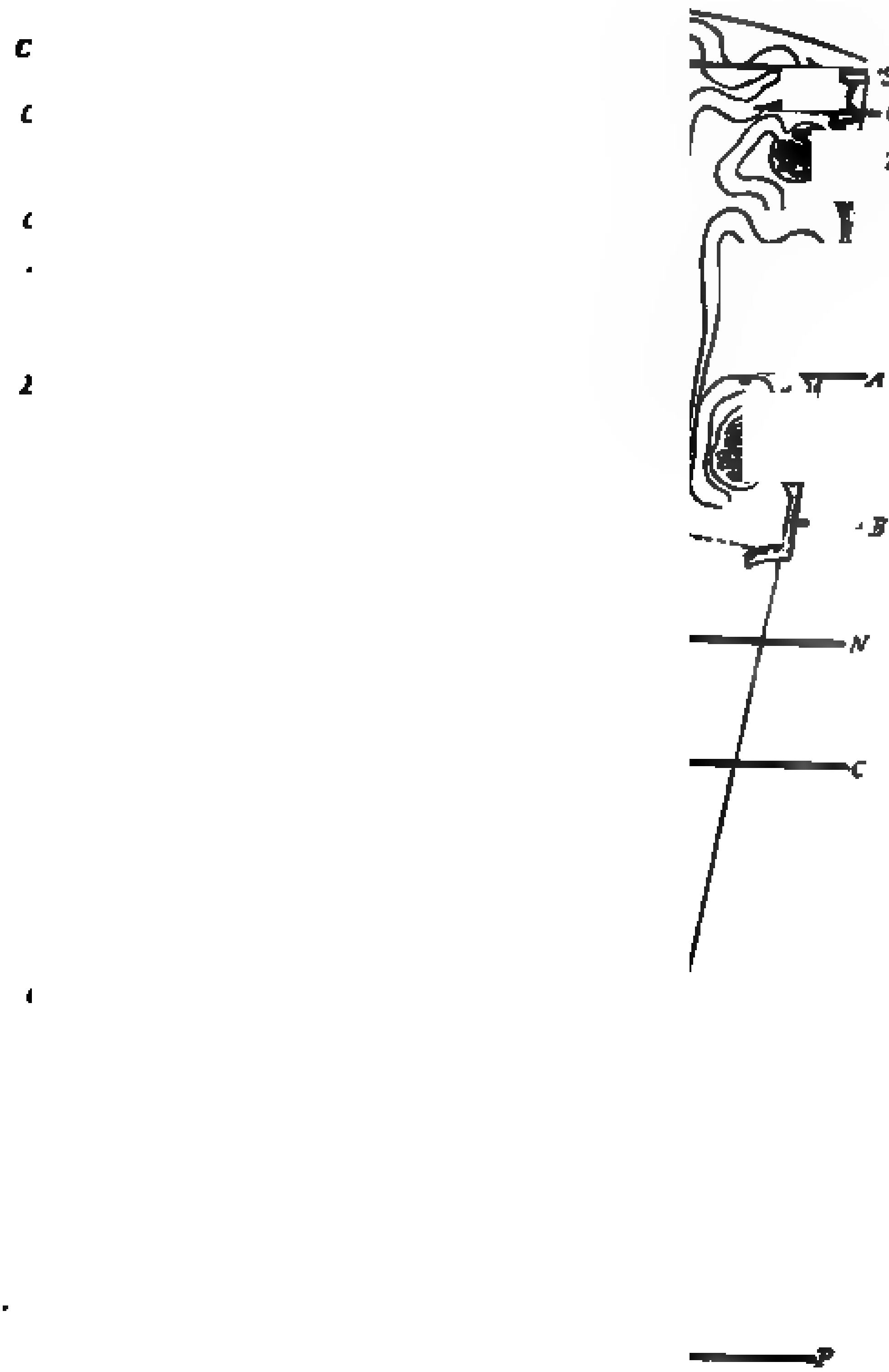

FIG. 333.—DIAGRAM OF THE KIDNEY.

A, renal artery, *V*, renal vein; *T*, tuft, *CT*, capsule of tuft; *AV*, afferent vessel. *EV*, efferent vessel. *CC*, capillaries of convoluted tubules, *CS*, capillaries of straight tubules. *B*, arterial branch to the cortical substance. *AP*, arterial branch to the pyramidal substance. *VR*, vasa recta; *CP*, capillaries of the straight collecting tubules. *L*, capillaries of the papilla, *CI*, convoluted tubule of the first order. *N*, narrow or loop-tubule, *CH*, convoluted tubule of the second order; *S*, straight collecting tubule in the medullary ray of the cortical substance; *C*, straight collecting tubule in the pyramidal substance; *P*, the same at the papilla.

certain depths in the pyramidal substance, the narrow tubule produces a *loop* (the loop of Henle), and takes an upward course as the *ascending branch* of the narrow tubule, this being on the whole slightly wider than the descending portion. Again, the ascending branch widens, with short, irregular curves and angles (the irregular portion), and at the most peripheral part of the cortex, in which there exist no tufts, it resumes the width and aspect of the convoluted tubule, being in this situation termed the *convoluted tubule of the second order*, or the intercalated tubule, which inosculates with the straight collecting tubule. By the union of several intercalated and collecting tubules arches are formed. Henle insists upon the arched arrangement of the collecting tubules themselves, to which the intercalated tubules are joined. The *collecting tubule* occupies the center of the medullary ray in the cortex. The groups of collecting tubes in the pyramis are situated between groups of the narrow tubules, decreasing in number, by continuous union at acute angles of analogous formations, until, lastly, a limited number of wide collecting tubules (eight to fifteen) open at the point of the pyramis —the papilla—which protrudes into the calyx. Their mouths are visible to the naked eye, and are called the foramina papillaria—the "blessed sieve" (cribrum benedictum) of old anatomists.

The uriniferous tubule may in its course, though not constantly, exhibit slight variations in its caliber and structure, and thus a number of subdivisions of their portions may be admissible. E. Klein, for instance, gives the following complex diagram of the course of a uriniferous tubule: (1) capsule of the Malpighian corpuscle; (2) narrowed neck; (3) the proximal convoluted tubule; (4) the spiral tubule of Schachowa, which is already part of the medullary ray; (5) the descending branch of Henle's loop; (6) the loop itself, which, turning upward and reaching the boundary layer, becomes suddenly enlarged and slightly wavy, thus forming (7) the first thick portion of the ascending limb of Henle's loop, and (8) the spiral part of the ascending limb; (9) then it becomes narrow again, and more or less straight or slightly curving; (10) produces the irregular tubule, with angular convolutions; (11) the intercalated segment; (12) the curved part of the collecting tube; (13) the straight part of the collecting tube of the cortex in the medullary ray; (14) the collecting tube enters the boundary layer, and lastly, the papillary portion; by confluence becomes (15) the large collecting tube, or tube of Bellini, until (16) it opens as one of the ducts on the free surface of the papilla.

Each portion of the uriniferous tubule has its peculiar epithelial lining. This, in general, can be defined as being *cuboidal* in the convoluted tubules, *flat* in the narrow tubules, and *columnar* in the collecting tubules.

The *convoluted tubules* of the first order, having an average diameter of 0.0045 mm., are lined by polyhedral epithelia, the cement-substance between them often being illy defined, or, especially in kidneys of children, absent. In these epithelia R. Heidenhain discovered a rod-like structure similar to that observed in the epithelia of the ducts of salivary glands. The ascending and descending portions of the *narrow tubules* have a diameter of 0.0020 to 0.0025 mm., and are lined by cuboidal epithelia, which also exhibit the rod-like structure; this peculiarity is particularly well marked in the irregular portions of the tubules. The descending portion gradually becomes narrow, and its epithelium passes by degrees into the flat variety, while the ascending portion often appears abruptly widened close above the loop, or in the depth of the loop itself. Along the course of the ascending tubule within the cortical substance the epithelium again may become flat, corresponding to a narrowing of the caliber. The narrow portions have a diameter of 0.0014; their caliber is comparatively wide, and the flat epithelia are finely granular and supplied with a distinct nucleus. In edge-view these epithelia appear spindle-shaped, closely resembling the endothelia of capillaries. The convoluted tubules of the second order have only a few convolutions; their caliber is somewhat wider than that of the convoluted tubules of the first order; their epithelia, however, being identical with those of the latter. In the irregularly winding portions the epithelia show slight differences in their depths. The collecting tubules have the widest caliber, their diameter being, at the apex of the medullary ray, the same as that of the convoluted tubules, while in their course toward the papilla they gradually assume a diameter of 0.020 to 0.030 mm. Their epithelia are at first cuboidal, but with increasing caliber the epithelia become distinctly columnar, being finely granular and obliquely arranged in the lower portions, after the manner of shingles on a roof. According to C. Ludwig, the membrana propria near the papillæ is fused with the surrounding connective tissue.

All tubular formations of the kidney are ensheathed by delicate connective tissue, which carries the blood-vessels and nerves. The peculiarities above described may be shown by antero-posterior (sagittal) sections of the kidney, which sever the tubules in a transverse direction. (See Fig. 334.)

Sagittal sections of the cortical substance will exhibit, within the medullary ray, transverse sections of the narrow tubules,

chiefly the ascending branches, and of the collecting tubules, all of which are fewer in number and of a less marked character the nearer the surface of the kidney, the main bulk of which is occupied by convoluted tubules. Sagittal sections of the pyramidal substance are characterized by bundles of the vasa recta arranged together with transverse sections of the narrow tubules, both the ascending, descending, and looped portion, around which are grouped the transverse sections of the collecting tubules. The narrow tubules become fewer, and the collecting tubules wider the nearer they approach the papilla. (See Fig. 335.)

Fig. 334.—Cortical Substance of the Kidney of a Dog. Sagittal Section. Blood-vessels Injected.

C, convoluted tubule; *N*, narrow or loop-tubule, *NA*, ascending branch of narrow tubule, *S*, straight collecting tubule. Magnified 300 diameters.

Of the *lymphatics* of the kidney very little is known. Some authors claim that they are clefts in the interstitial connective tissue, while others describe rhomboidal meshes of lymphatics, bounded by an endothelial coat, around the uriniferous tubules. In the capsule of the kidney there is a regular lymphatic system, and in the hilus several large lymph-vessels are found which are supplied with valves.

The *nerves* of the kidney have been, for a number of months, studied in my laboratory by Dr. M. Holbrook, who has not yet completed his researches. He found a large number of nerves accompanying the arteries and producing a reticulum around the capillaries, in accordance with the statements of L. Beale. Every tubule is accompanied by a reticulum of non-medullated nerve-fibers, from which prolongations pass through the basement-membrane, and produce a very narrow plexus close above this membrane. From the intra-tubular plexus delicate branches arise, running along the cement-substance of the epithelia, and in union with the slender, transverse filaments traversing the cement-substance and inter-connecting the epithelia. Such fibrillæ are represented in Fig. 337. By Holbrook's specimens it is plainly shown that every epithelium is in connection with a

nerve-fiber, though this connection is indirect through the inter-epithelial filaments of living matter (the so-called thorns). It could not be demonstrated that the nerve-fibrillæ penetrate the interior of the epithelia.

Researches in the Minute Anatomy of the Epithelia of the Kidney. By Henry B. Millard, A. M., M. D.*

R. Heidenhain † was the first to call attention to the presence of a peculiar rod-like or bacillated structure existing in the uriniferous tubules. He found this structure in convoluted tubules, in the ascending portions of the looped

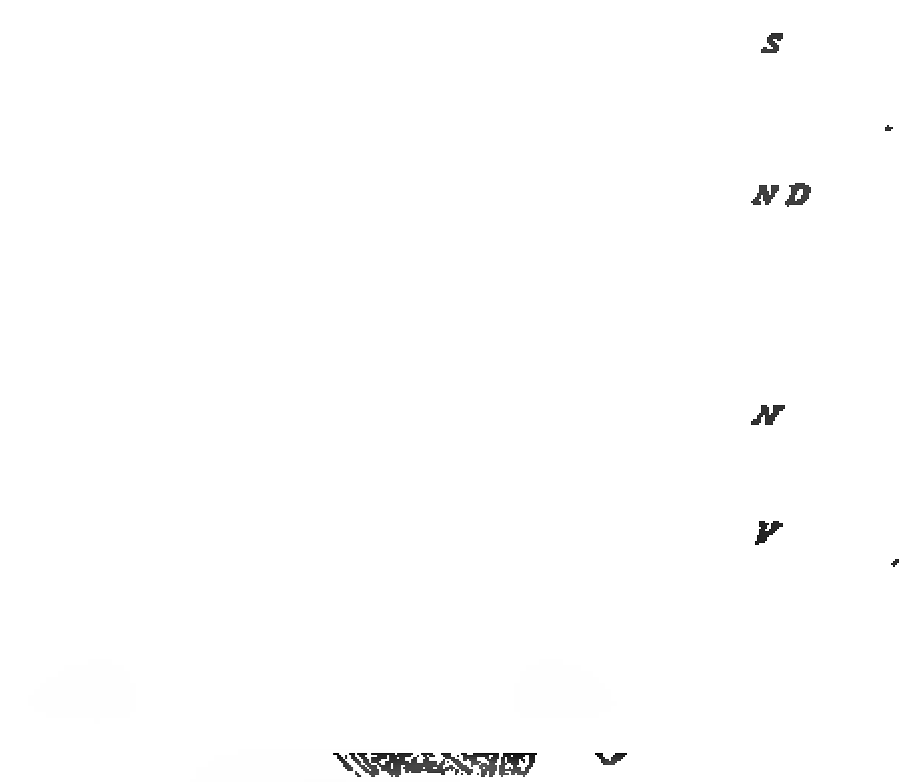

Fig. 335.—Pyramidal Substance of the Kidney of a Dog. Sagittal Section. Blood-vessels Injected.

N, narrow or loop-tubule; *ND*, descending branch of narrow tubule; *S*, straight collecting tubule; *V*, vasa recta. Magnified 500 diameters.

tubules, and in the intercalated tubules of the kidneys of mammals. According to his view, the rodlets (Stäbchen) are plainly visible in the outer portions of the epithelia — that is, in those portions lying next the connective tissue, and he sometimes saw in torn epithelia the rods isolated. The same observer‡ also first demonstrated with accuracy that the secretion of the salts is performed only in the tubules, in accordance with the views maintained by Bowman. Charcot § deduces from the experiments of Heidenhain with indigo-blue

* Abstract of the author's essay *The New York Medical Journal*, June, 1882.

† "Mikrosk. Beiträge zur Anat. und Physiologie der Nieren." Max Schultze's "Arch. f. mikr. Anat.," 10 Bd., 1874.

‡ "Versuche über den Vorgang der Harnabsonderung." Pflüger's "Archiv," 9 Bd., 1874, page 1.

§ "Charcot on Bright's disease," translated by Millard, New-York, 1878, page 23.

the conclusion that the secretion or elimination of this coloring matter takes place only in those portions of the tubuli uriniferi which are covered by the epithelia having the rods (épithélium à bâtonnets). Whether the secretion of the specific principles of the urine takes place in precisely the same fashion as the elimination of coloring matters, he regards as impossible of demonstration experimentally. In a recent monograph, Charcot * regards the *tubuli contorti* and the loops of Henle, particularly the ascending branches of the loops, as the real glandular part of the kidney. Heidenhain, however, did not associate the rods with the process of secretion, for he observed a similar structure also in the smaller ducts of the parotid and submaxillary glands, the same formation in the latter structure being already known to Henle and Pflüger. In the acini of the glandula submaxillaris and in the other acinous glands he could not discern them. E. Klein † asserts having observed that the rods or fibrils of Heidenhain, when looked at from the surface, are connected into a net-work, so that they are more probably septa of a honeycombed net-work seen in profile. What the intimate nature of these formations is, neither of the above-named authors attempts to explain.

Since the reticular structure of all protoplasmic formations, including therefore epithelium, was demonstrated by C. Heitzmann, the question has been, what the reticulum present in the protoplasm is. A proof of the reticulum being the living matter proper rests upon the fact that, both in normal and in morbid processes, the new formation of corpuscular elements starts from the points of intersection in the reticulum. This so-called endogenous new formation of living matter is especially plain in the inflammatory process invading epithelial formations. Here, it is important to note, the reticulum at first becomes coarse; next, it coalesces into lumps, which, being at first homogeneous, in turn assume a reticular structure themselves, and now represent so-called inflammatory or pus-corpuscles. These corpuscles at first remain in connection with the neighboring reticulum by means of delicate filaments, which are portion and part of the reticulum. Later, when the inflammatory corpuscles which have originated in the interior of an epithelium become extruded from its interior, the newly formed corpuscles represent pus-corpuscles.

In conducting my researches, I have studied the kidneys of the rabbit, pig, dog, and man, all of them being preserved and hardened in a solution of chromic acid. I have, therefore, no observations to report upon the form-changes of the epithelia, but have studied the changes in the interior structure of the epithelia in the inflamed human kidney. These investigations enable me to maintain that the reticular structure of the epithelium of the kidney *is really a formation of living matter.*

Upon closely examining the epithelia of the tubuli uriniferi in the kidneys of the above-named animals, we readily perceive, with comparatively low powers of the microscope (400 or 500 is sufficient), the presence of rod-like formations in the epithelia of the *tubuli contorti*, in the irregular tubules, in the ascending branch of the looped tubules, and in the intercalated tubules, entirely in accordance with Heidenhain's assertions. The drawings of the rodlets, as given by Heidenhain and copied by Klein and other writers, give an exaggerated idea of the real appearance of the rods. Even under a high

* "Leçons sur les Conditions Pathogéniques de l'Albuminurie," Paris, 1881.
† "Atlas of Histology," London, 1880.

power they are never so large as in the drawings, and seldom present the straight, regular, and symmetrical appearance there represented.

The pale, flat epithelia of the looped tubule proper do not, as a rule, exhibit the rods. The columnar epithelia of the collecting tubules, on the contrary, which are distinctly imbricated, especially in the kidney of the dog, exhibit the rods more or less plainly. The columnar epithelium of the rabbit does, however, show them.

High powers (1000 to 1200) of the microscope corroborated the views of Klein—namely, that the rods are connected into a reticulum by means of delicate filaments inosculating both with the wall of the nucleus around which the rods are located, and also with the delicate reticulum in the inner portion of the epithelia, next to the caliber, where the rods are usually absent. It is striking how the thickness of the rods differs in the different epithelia of the same animal's kidney. Sometimes they are very thin, beaded poles, with quite distinctly marked interstices between them. In this case the connecting filaments, running almost at right angles from rod to rod, are easily discernible. At other times the rods are rather bulky formations, having but extremely narrow interstices between them. In this instance the connecting filaments, as a matter of course, are very short, and not easily seen. In a third instance the outermost portion of the epithelium is a compact or homogeneous mass, in which no rods can be observed at all. (See Fig. 336.)

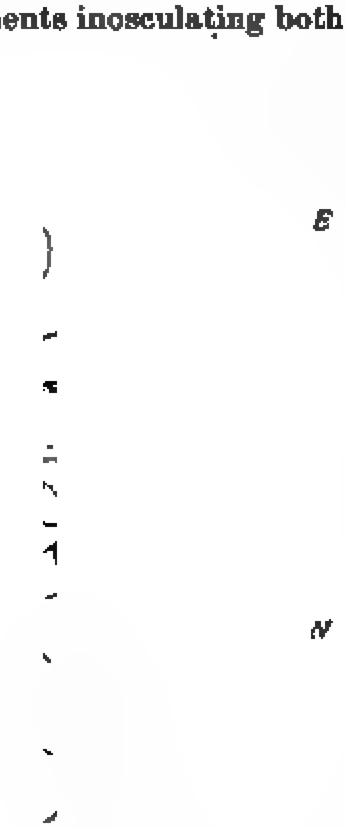

FIG. 336.—CONVOLUTED TUBULE FROM THE KIDNEY OF A RABBIT. LONGITUDINAL SECTION.

N, nucleated columnar epithelium, showing the rods. *E*, endothelia, *I*, interstitial connective tissue, producing the basement-layer. Magnified 1200 diameters.

Another striking feature is the great variety of appearances exhibited by the cement-substance. Sometimes this is plainly marked at regular intervals between the epithelia. Then the transverse connecting filaments, the formerly so-called thorns, are plainly visible. At other times hardly any trace of cement-substance is seen, but the reticular structure is present in a nearly uniform distribution throughout the epithelial layer. Where the rods are slender, the nucleus, as a rule, is well defined; where, on the contrary, they are bulky, the nucleus is, on an average, not very plainly marked. The sharpest definition of the nucleus is furnished by the flat epithelia of the looped tubules in which the rods are absent.

In inflamed kidneys of man I have repeatedly found the rods. Here the rods of the epithelia throughout the tubules are clumsy and bulky, the whole reticulum being enlarged, rendering the epithelium, with low powers of the microscope, coarsely granular. In many instances the rods are not discernible, as, in their place, a coarsely granular mass is present, pervading the whole epithelial body; or else the innermost portion of the epithelium looks coarsely

granular, the outermost portion, on the contrary, being homogeneous and shining. I have repeatedly seen, in acute interstitial nephritis, even the looped tubules, which in this situation were considerably increased in bulk, provided with a coarsely granular reticulum — nay, even with an indistinct, rod-like structure. All these features become still more prominent by staining the specimens with the chloride of gold after they have been soaked and washed for several days in distilled water. This reagent, in a half per cent. solution brought in contact with the specimens for forty minutes, renders sections from the normal kidney of a brown-violet hue, slightly increasing the distinctness of the reticular structure of the epithelia. In the inflamed kidneys of man, the epithelia of a great many of the ascending, irregular, and convoluted tubules, upon being stained with the chloride of gold, as above described, became dark violet. With higher powers of the microscope we can ascertain that it is the coarse reticulum, the bulky rods, and the homogeneous masses sprung from coalescence, as it were, of the rods, which exhibit the deepest gold stain.

As it is the tubuli uriniferi which have the rod-like structure, which in Heidenhain's experiments with indigo sulphate are the only ones which are colored by it, so in the inflamed kidney it is only these tubules that become colored by the gold. It seems reasonable to suppose, from the effect of these reagents, that the epithelia with rods, perhaps by virtue of their having more living matter and a more bulky reticulum, are of most importance in secreting or forming the extractive matter of the urine.

In the inflamed kidneys, in which the violet coloration was produced, no doubt the reticulum of the epithelia, owing to the inflammatory process, was considerably increased in bulk. The most marked violet stain was exhibited by a number of the convoluted tubes and by irregular and ascending tubules. We know that living matter is considerably increased in amount in the inflammatory process, and are justified, consequently, in maintaining that the reticulum and the rod-like formations within the epithelium, being part of the reticulum, are formations of living matter. (See Fig. 337.)

As to the significance of the rods, it may be inferred that they are in close relation with the process of secretion. Obviously, the stream of liquid running from the neighboring blood-vessels through the epithelia toward the liquids contained in the caliber, and *vice versa*, will be facilitated by an elongated arrangement of the reticulum — *i. e.*, the rods. In a state of comparative rest the rods lie close to each other — nay, are coalesced into homogeneous masses. In this condition the cement-substance between the epithelia is best marked. In full activity of the epithelium, on the contrary, the rods will be very distinct, will stand farther apart, and the cement-substance between the epithelia will, in consequence, become indistinct.

The Endothelia of the Urinary Tubules. While investigating the peculiarities in the structure of epithelia of tubuli uriniferi in their normal condition, I often observed the presence of flat, spindle-shaped bodies between the basis of the epithelia and the adjacent so-called structureless membrane of the tubule. These spindle-shaped bodies doubtless correspond to those flat, nucleated formations which cover the inner surface of the structureless layer in nearly all epithelial — *i. e.*, glandular — formations. By most observers they are regarded as endothelia belonging to the connective tissue subjacent to the epithelial layers. V. Czerny was the first one to bring them to view in other tissues, which he did by staining the specimens with the nitrate of

silver; and C. Ludwig,* also by the silver stain, first indicated their presence in the urinary tubules.

Such an endothelial layer, present in all varieties of the urinary tubules, is best visible in the front view of the structureless membrane, where the epithelium is stripped off. Here the endothelia are comparatively large, irregularly polyhedral bodies, with distinct central nuclei. The nucleus has a plainly marked shell, containing in its interior a few small nucleoli, the nuclei being mostly of oblong shape. In the body of the endothelium a delicate reticulum is seen with very minute nodulations. Each body is separated from all its neighbors by a delicate light rim of cement-substance, which is traversed at right angles by extremely minute filaments or thorns. In side view, obviously, these bodies will exhibit a spindle-shape, the broadest portion of the spindle corresponding to the central nucleus.

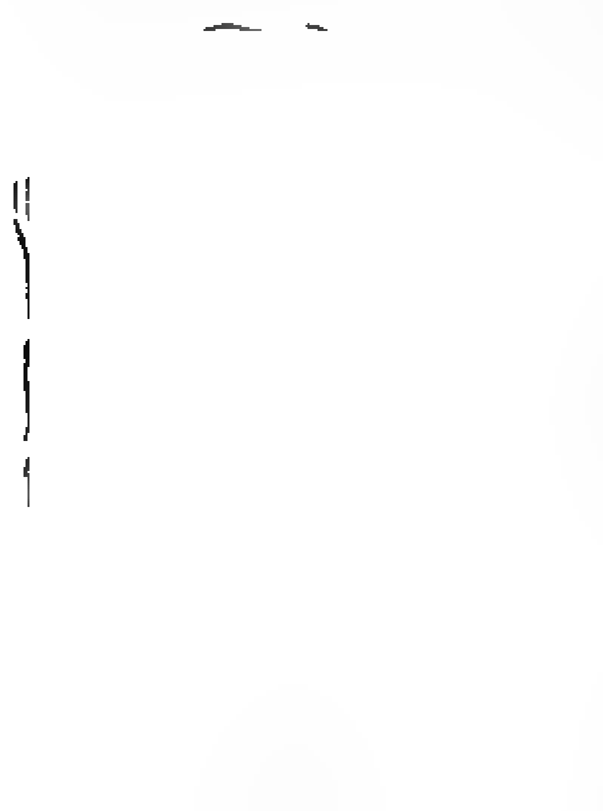

FIG. 337.—CONVOLUTED TUBULE FROM A HUMAN KIDNEY AFFECTED WITH ACUTE CATARRHAL (INTERSTITIAL) NEPHRITIS. OBLIQUE SECTION.

P, Inflammatory corpuscle, sprung from the division of an epithelium; *D*, cluster of inflammatory corpuscles, sprung in the same manner; *R*, rods of cuboidal epithelia, still recognizable; *E*, endothelia, increased in size and number. Magnified 1200 diameters.

If the views of recent observers are correct—namely, that the structureless layer, synonymous with the hyaline or basement-layer, is an aggregation of endothelia infiltrated with elastic substance—this view may also be applied to the structureless membrane of the urinary tubules. In normal kidneys I failed to discover nuclei in the structureless layer proper, which would indicate their construction of former endothelia. In inflamed kidneys, on the contrary, no doubt was left as to the fact that the structureless layer is composed by a number of closely attached, in part nucleated, endothelia.

In the inflamed kidney the endothelial layer beneath the epithelial is always more marked than in the normal kidney. In chronic catarrhal (interstitial or desquamative) nephritis, all the tubules that have lost their epithelial investment invariably show an investment of endothelia.

This, in the transverse section of the tubule, is characterized by the presence of flat, irregularly spindle-shaped bodies, which are always more coarsely granular than in the physiological condition. Their nuclei are also more coarsely granular, sometimes homogeneous. The flat shape, the large size in the frontal diameter, and the construction of the nuclei serve for an accurate contradistinction to epithelia. I have failed in obtaining specimens indicative

* "Hand-book of Histology," by S. Stricker, London, 1874.

of a new formation of epithelia after the loss of the original epithelial investment. (See Fig. 338.)

It may be admissible to assume that the enlarged endothelial layer serves (at least to some extent) as a substitute for the lost epithelia. In tubules whose epithelia, as in chronic catarrhal nephritis, are transformed into inflammatory or medullary corpuscles, the new formation of such structures also starts from the endothelia. The final result in this instance is known to be the destruction of the tubule and its replacement by newly formed connective tissue—a condition which is known by pathologists as cirrhosis of the kidney.

Still more plainly marked are the endothelia in croupous (parenchymatous) nephritis. In fact, the appearances seen in urinary tubules, where casts have just formed, could not be explained, unless by the presence of endothelia. We do not yet know what the mass composing a cast really is. This much, however, is certain, that casts are proteinates and formations of an albuminous or fibrinous exudate from the blood-vessels. This exudate, before it reaches the central caliber of the tubule, necessarily must saturate the intervening epithelia, whose structure is completely destroyed by this process.

FIG. 338.—CONVOLUTED TUBULE FROM A HUMAN KIDNEY AFFECTED WITH CHRONIC CATARRHAL (DESQUAMATIVE) NEPHRITIS. OBLIQUE SECTION.

C, caliber, widened by loss of the epithelia. *E*, endothelia, increased in size and number. *F*, interstitial fibrous connective tissue, with augmented plastids. Magnified 1200 diameters.

It is not my purpose to dwell upon the origin of casts; but, from what I have seen, I cannot concur with Oedmansson * in the opinion that every cast should be regarded as a product of secretion furnished by the epithelium. I am sure that the epithelia perish in the formation of the cast. Neither can I agree with Charcot † in the opinion that some (granular) casts are made up of broken-down epithelial cells, others (hyaline and some granular) of an albuminous substance, while epithelial casts are agglomerations of epithelial cells more or less altered. Bartels ‡ insists that, in every case in which he has examined microscopically thin sections of diseased kidneys whose tubules were blocked by the dark granular casts, the tubules invariably exhibited an epithelial lining, reconciling this fact with his view by admitting that the theory of Key and Bayer—that the epithelium thus shed is rapidly reproduced—may be correct. From my observations it is obvious that the

* Bartels, von Ziemssen's "Cyclopædia," vol. xv., pp. 84.
† Charcot, "Bright's Disease." Millard's translation, New-York, 1878, pages 29 *et seq.*
‡ Bartels, *op. cit.*, pp. 84–86.

last three writers have regarded the endothelia, as I have described them, as epithelia.

Whenever we find a cast within a tubule, especially in transverse sections of the tubule, we almost invariably see a wreath of irregularly spindle-shaped, partly nucleated bodies, which I am sure are nothing but the lining endothelia of the structureless membrane. Alfred Meyer * gives illustrations of these wreaths, which evidently are drawn with the greatest accuracy; but he does not realize at all their character or significance, for he suggests that they are constructed either of remnants of the former epithelia, of which a large portion has been destroyed in the formation of the cast, or that they may be newly formed epithelia. In both these views he is mistaken. The epithelia are certainly gone, entering, in a considerably swollen condition, the mass of the cast, and what is behind the cast is not newly formed epithelia, but merely the endothelial investment of the structureless layer, considerably increased in size. (See Fig. 339.)

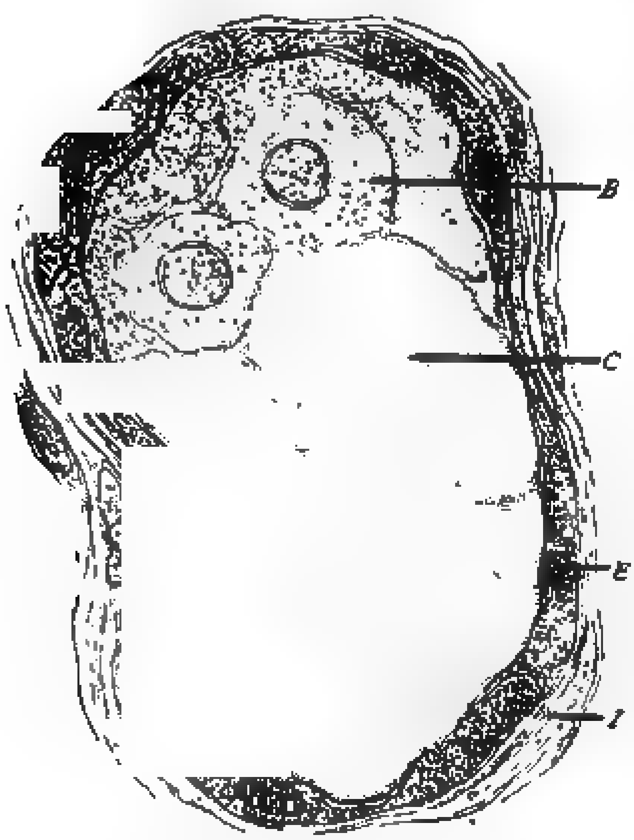

FIG. 339.—CONVOLUTED TUBULE FROM A HUMAN KIDNEY AFFECTED WITH ACUTE CROUPOUS NEPHRITIS. OBLIQUE SECTION.

C, hyaline cast. *B*, swollen and disintegrated epithelia participating in the formation of the cast. *E*, wreath of endothelia. *I*, interstitial connective tissue. Magnified 1200 diameters.

Not infrequently we see widened urinary tubules—as a rule, of the convoluted variety—entirely destitute of epithelia; or we see such tubules containing a cast broader in its diameter than the caliber of the tubule would be if the epithelial layer were present. The latter feature is explicable by the fact that casts may be carried into tubules far distant from the place of their origin—into tubules, besides, which have been previously deprived of their epithelia. There is no cogent necessity whatever for the conclusion that casts may form in tubules after these have lost their epithelia. In neither of these instances shall we ever miss the endothelial investment, although this is often found in a mutilated or imperfectly developed condition.

The results of my researches may be summed up in the following statements:

1. *The rods discovered by Heidenhain in some varieties of the tubuli uriniferi are part and parcel of a reticulum present within every epithelium.*

2. *The reticulum, including its elongated, rod-like formations, is the living matter proper.*

* "Untersuchungen über acute Nierenentzündung." "Sitzungsb. d. Akad. d. Wissensch. zu Wien," 1877.

3. *The relation of the rods to the rest of the reticulum of an epithelial body varies greatly, the variation probably being due to different stages or degrees of secretion.*

4. *The reticulum, including the rod-like formations, in the inflammatory process, both in catarrhal and croupous nephritis, gives rise to a new formation of living matter, which results in the new formation of medullary corpuscles or pus-corpuscles.*

5. *The structureless membrane is lined by flat endothelia lying between it and the basis of the epithelia of the urinary tubules.*

6. *In nephritis the endothelia become considerably enlarged, and in catarrhal, as well as in croupous nephritis, they line the urinary tubules after the epithelia have been shed or lost; they surround the cast in croupous nephritis after the epithelia have perished in the formation of the cast.*

Nephritis. Under the head of *Bright's disease* are included a number of morbid processes of the kidneys which comprise mainly acute and chronic inflammation and its terminations. No clear understanding of nephritis was hitherto possible on account of the lack of discrimination between its different forms and degrees, although this disease is far more common than is usually thought, as proved by the careful examination of the urine of even apparently healthy persons. Every acute or chronic disease of the organism, terminating fatally, reflects upon the kidneys to such an extent that, with the exception of sudden and accidental deaths, normal kidneys are never found on autopsy. In three hundred post-mortem examinations of persons dead of tuberculosis in its manifold appearances, I have never met with perfectly healthy kidneys; and in most the cases of persons dead of different acute or chronic diseases, the kidneys were also found in a pathological condition—at least, so far as the examination with the naked eye admitted of conclusions.

Instead of the more modern terms interstitial, desquamative, parenchymatous nephritis, and the insignificant term Bright's disease, involving all varieties of nephritis, I prefer to adopt the old-fashioned terminology of humoral pathology. As explained in previous chapters, every inflammation of glandular organs is interstitial, desquamative, and parenchymatous, as the process starts in the vascularized connective tissue and the epithelia participate, as it were, in a secondary way. I distinguish different degrees of nephritis, which are: *the catarrhal, the croupous,* and *the suppurative,* each of which may be acute, or chronic, or subacute — *i. e.,* chronic with repeated acute recurrences.

The two following articles are the results of careful researches made on a large number of kidneys both of human beings and of animals. They throw light upon the hitherto dark subject of

nephritis, especially so the article on chronic nephritis, which is based on researches extending over years. The secondary changes of the kidney-tissue, embracing the formation of cysts, the fatty and waxy degeneration, are cleared up in a satisfactory manner.

Here I briefly wish to allude to the peculiar formations, termed tubular casts, which are observed under the microscope in the urine as well as in the tubules of the kidneys. They were first described as occurring in both situations by Henle in 1842, who considered them to be coagulated fibrine. Since that time the views concerning their origin have greatly changed; they were considered as products of secretion of the epithelia of the tubules, or as transformed epithelia, but the participation of the blood in the formation of casts was neglected. N. A. J. Voorhoeve,* in an excellent article, gives the results of experiments made for the purpose of tracing the origin of the casts in the tubules. This author produced casts in rabbits' kidneys by administration of cantharides and of neutral chromate of ammonia, and by ligation of the ureters, and especially by a temporarily impeded circulation in the kidneys through compression of the renal artery and the renal veins. He comes to the conclusion that only the dark granular casts are due to a disintegration of the tubular epithelia, while hyaline casts are caused by disturbances in the vascular system, without the least participation on the part of the epithelia. He claims having observed within the tubule the epithelial wreath around each cast. Numerous observations in inflamed kidneys led me to the conclusion that the wreath of partly nucleated flat bodies around the casts are not epithelia, but the grown-up endothelia, subjacent to the epithelial cover, while the epithelia, being saturated with an exudate from the neighboring blood-vessels, are transformed into the mass composing the cast. How this conception has developed is shown by the foregoing and the two following articles. A simple hyperæmia of the kidneys cannot, as is generally believed, lead to the formation of the casts, as they are always the products of an inflammatory action, which is also well marked in the surrounding connective tissue. Voorhoeve's experiments elucidate the probable source of nephritis in pregnancy, which in all evidence is caused by a pressure on the renal vein of the pregnant uterus, mostly in the right kidney.

Nephritis, as every other disease, is marked by various degrees

* "Ueber des Entstehen der sogenannten Fibrincylinder." Virchow's Archiv, LXXX. Bd., 1880.

of intensity. Sometimes it appears in a mild form, not seriously interfering with the general health of the person, while in other instances it destroys life in a very short time. The presence of casts in the urine I consider a serious symptom, though, if present only in small numbers, they indicate a slight inflammatory disturbance in the kidneys, which might run for quite a number of years.

As the uriniferous tubules are lined with only a single layer of epithelia, a perfect recovery from any attack of nephritis must depend upon the reproduction of the lost epithelia from those which remain. Nothing is known concerning the reproductive power of kidney epithelia, and that it occurs is a mere inference. Patients overcome milder attacks of *catarrhal nephritis;* but the danger rests in repeated recurrences of this nephritis, which at length leads to cirrhosis of the kidneys. Recovery after *croupous nephritis* seems in children to be complete — f. i., after scarlet fever or diphtheria. They sometimes overcome acute hæmorrhagic croupous nephritis of a degree which invariably kills the adult. Recovery, furthermore, is often observed after the nephritis of pregnancy, probably for the reason that only the right kidney is the seat of disease. Nephritis produced by certain poisonous drugs (cantharides, turpentine, etc., often, also, iodine and arsenical preparations) may terminate in a cure as soon as the administration of the poison is stopped. Even chronic nephritis, with waxy degeneration, will, if caused by chronic pyæmia, subside after the removal of the source of suppuration. In such cases of recovery certain regions of the original kidney-tissue are destroyed, and replaced by cicatricial connective tissue, producing a condition of atrophy in those portions, while the greater part is left unchanged. In most instances of spontaneous croupous nephritis, however, the disease becomes chronic, with repeated attacks of intercurrent acute nephritis, and terminates finally in a partial atrophy of the kidney-tissue, or a general hypertrophy of the interstitial connective tissue. Such kidneys are usually subject to cystic, fatty, and waxy degeneration. Whether or not the two last-named conditions arise primarily, without any preceding inflammation, I am unable to say.

ACUTE INFLAMMATION OF THE KIDNEYS. BY ALFRED MEYER, NEW-YORK.*

Since Richard Bright, in 1827, drew attention to certain diseases of the kidneys, in consequence of which severe disturbances of the organism, and

* Abstract of the essay, "Untersuchungen über acute Nierenentzündung." Sitzungsber. d. Kais. Akademie d. Wissensch. in Wien, LXXV. Bd., 1877. Translated by the author.

not infrequently death, could be produced, leading pathologists have retained the designation "Morbus Brightii," and distinguished it from nephritis. Thus, C. Rokitansky* separates nephritis from Bright's disease. P. Rayer,† and subsequently B. Reinhardt,‡ described Bright's disease as a diffuse exudation into the renal tissue. Frerichs § likewise regarded the designation "inflammation of the kidney" as insufficient, and retained the customary name of "Bright's disease." Virchow ‖ was the first to speak of a catarrh of the urinary tubules, and to know that the catarrh could increase to croup—that is to say, to the formation of a fibrinous exudation in the urinary tubules. According to him, croup of the urinary tubules is a severer degree of catarrhal inflammation. As a third form he adopts "parenchymatous inflammation" of the kidney, which depends essentially on a change in the epithelial cells. In his opinion, catarrhal, croupous, and parenchymatous inflammation can attack the kidney simultaneously, and for this condition he wishes to retain the name of "Bright's disease." Herewith, the way was prepared for the idea that Bright's disease is an inflammatory process, and this view was subsequently adopted by the following authors: S. Rosenstein,¶ who speaks of a catarrhal and of a diffuse nephritis; furthermore, William Aitken[1] and J. Hughes Bennett.[2] Aitken distinguishes two varieties of inflammation of the kidney, in Virchow's sense,—namely, the interstitial, in which, principally, the connective-tissue stroma is diseased, and the parenchymatous, in which the urinary tubules are mainly affected. T. Grainger Stewart[3] divides this disease into an inflammatory, an amyloid, and a cirrhotic form. Ed. Rindfleisch[4] declares premature the attempts of Rayer, Foerster, and others to draw sharp lines between a simple albuminous, a parenchymatous, an interstitial, and a croupous nephritis. He speaks of a desquamative catarrh, of an acute parenchymatous nephritis,—under which latter head he distinguishes between a circumscribed purulent, and a diffuse, non-purulent form. In addition, he speaks of a combination of parenchymatous and interstitial nephritis. C. Heitzmann[5] asserts that the picture of Morbus Brightii drawn by Rokitansky includes two different forms, namely, croupous and interstitial nephritis. According to him, the characteristic anatomical feature of interstitial nephritis is the striation of the more or less swollen cortical substance; while the characteristic feature of croupous nephritis depends on the diffuse infiltration, superadded to the inflammatory swelling and redness. C. Bartels[6] divides the diffuse diseases of the kidney into hyperæmia, ischæmia, parenchymatous inflammation, interstitial inflammation, and amyloid degeneration.

This much is clear at the present day, that the designation "Bright's disease" must be dropped as being altogether unscientific. Virchow's

* "Handbuch der Pathol. Anatomie," 1861, 3 Aufl.
† "Traité des Maladies des Reins," Paris, 1840.
‡ "Annalen des Charité Krankenh., Berlin, 1850.
§ "Die Bright'schen Nierenkrankheiten und ihre Behandlung," Braunschweig, 1851.
‖ "Ueber parench. Entzünd." Virchow's Archiv, 1852.
¶ "Die Pathol. und Therap. der Nierenkrankheiten," Berlin, 1870.
[1] "Science and Practice of Medicine," London, 1863.
[2] "Principles and Practice of Medicine," Edinburgh, 1865.
[3] "A Practical Treatise on Bright's Diseases of the Kidneys," Edinburgh, 1871.
[4] "Lehrbuch der Pathologischen Gewebelehre," 3 Aufl., Leipzig, 1873.
[5] Ueber Tuberkelbildung. Wiener Med. Jahrb., 1874.
[6] "Krankheiten des Harnapparates in Ziemssen's Handbuch der spec. Pathol. und Therap." Leipzig, 1871.

attempt to localize the inflammatory processes (which, as generally agreed, form the basis for all the changes of renal tissue described as Bright's disease) in the principal histological components of the kidney, namely, in the tubular epithelium, in the blood-vessels, and in the connecting stroma, cannot be carried out. I am not familiar with any form of inflammation, whether of the kidney or of any other glandular organ, which can begin and also run its course in only a single one of the constituent tissues. Under all circumstances every one of the histological components is involved in the process, not only in the mildest catarrhal inflammation, but also in the severe form of suppuration.

To me no other method of elucidating the forms of renal inflammation seems possible than a comparison with analogous processes in glandular organs in general, whose simplest representatives are the mucous membranes. If we remember that in inflammation the blood-vessels are implicated by the production of an exudate, and the other histological constituents by morphological changes brought about by nutritive disturbances of the living matter, we shall have to regard every inflammatory process as a disease of the tissue in its entirety. Neither the blood-vessels, nor the connective tissue, nor the epithelium alone can exclusively afford the substratum of an inflammatory process, but always these components coincidently. Whatever in the tissue is endowed with life will become active and then productive during a nutritive disturbance, and only in the case of the death, of the so-called gangrene of the tissue is the idea admissible that the tissue is destroyed and remains passive.

In analogy to the varieties of the inflammatory processes in mucous membranes, we may also speak of a catarrhal, croupous, suppurative and diphtheritic inflammation of the kidney. Each of these varieties may be circumscribed or diffuse; each can gradually pass into the other without our being able to draw sharp lines between them, either with the naked eye or with the microscope.

We will accordingly retain this principle of division. The term "croupous nephritis" has been declared to be inadmissible, because the fibrinous nature of the casts, and hence their identity with the croup membrane of other mucous membranes has not been demonstrated. True, croup-membrane and casts are neither morphologically, nor microscopically, nor chemically entirely identical. I shall however, try to explain these differences and believe that I am justified in upholding the variety of croupous nephritis on account of all its accompanying conditions. I shall not consider the diphtheritic variety of inflammation, since it mainly affects the renal pelvis and calices.

(1) *The Catarrhal (Desquamative, Interstitial) Nephritis.* The phenomena which are characteristic of mild catarrhal inflammation in a mucous membrane are œdematous swelling of the connective tissue, swelling and granular cloudiness of the epithelial covering, and subsequent desquamation of the epithelium. The blood-vessels which, even to the naked eye, appear filled and dilated, under the microscope show a more or less complete distension with blood-corpuscles, without apparent alteration in the structure of their wall. It never has been doubted that the œdematous swelling of the connective tissue and the desquamation are due to a serous exudation from the blood-vessels, in spite of the fact that the exudation, as such, cannot be seen under the microscope. The presence of the exudate within the tissue (paren-

chymatous and interstitial exudation, Virchow) is to be regarded as an essential factor of the inflammatory changes, since partly mechanical changes and partly nutritive disturbances are produced by it.

In more severe and prolonged acute catarrhal inflammation the connective tissue participates in what is called "inflammatory infiltration," which leads to hypertrophy (hyperplasia). It is a well-known fact that the changes in the connective tissue are accompanied also by changes in the epithelium — viz. at first, proliferation, then desquamation, and finally, hyperplasia of the epithelium.

Thus, the catarrhal inflammation in the kidney consists, in the beginning principally in changes of the epithelia, subsequently in changes of the connective tissue. For this reason, a subdivision into epithelial changes (parenchymatous, Virchow) and connective tissue changes (interstitial, Virchow) is not admissible. Catarrhal inflammation includes, with only gradual differ-

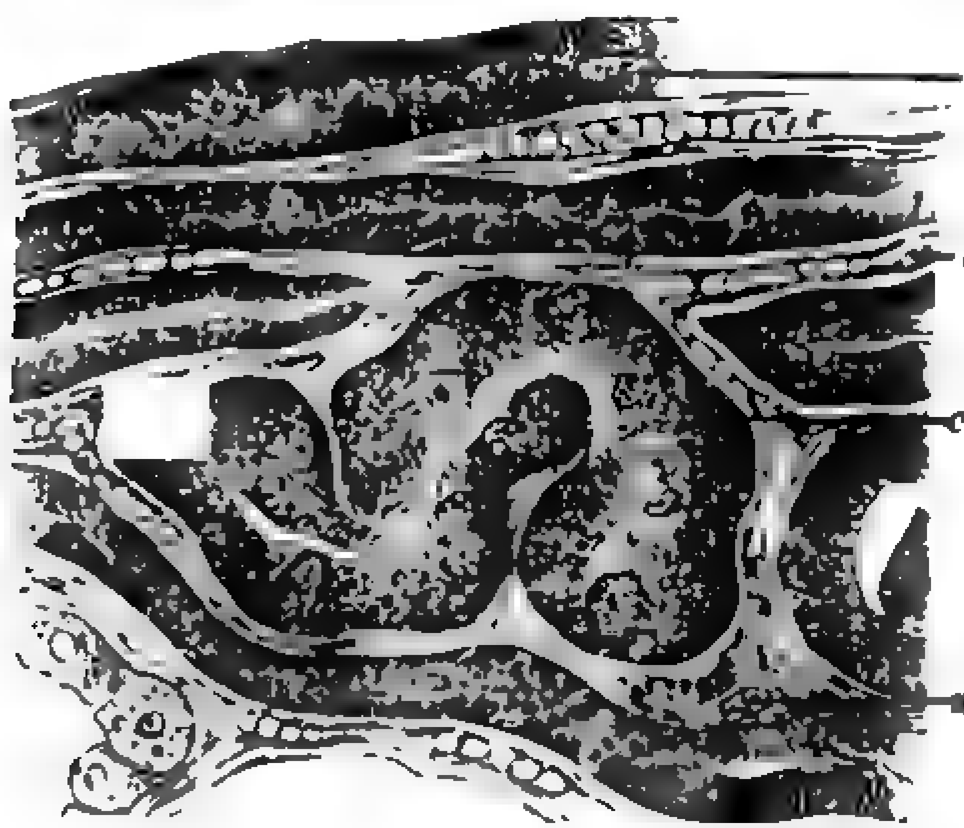

FIG. 340.—ACUTE CATARRHAL NEPHRITIS. INITIAL STAGE.

C, convoluted tubule. *N*, ascending branch of narrow tubule. *I*, interstitial connective tissue in œdematous swelling. *M*, beginning of inflammatory infiltration. Magnified [illegible] diameters.

ences, the desquamative, the interstitial, and also the parenchymatous form of inflammation described by authors.

I have studied acute catarrhal inflammation in the kidneys of a child six years of age, dead of diphtheria, in which symptoms of uræmia had ensued four or five days before death. The changes implicated principally the cortical substance. (See Fig. 340.)

Some capillaries are choked with red blood-corpuscles and dilated, others hold a moderate amount of blood. Some blood-vessels contain, besides indistinctly recognizable red blood-corpuscles, a finely granular material, which corresponds, perhaps, to what authors call "micrococci." Since the inference

drawn nowadays from the presence of such micrococci in certain forms of nephritis cannot be regarded justifiable, I am satisfied with the statement of the above condition. The majority of the glomeruli are moderately enlarged and their vessels provided with more abundant bodies resembling nuclei than normal; I cannot decide whether these changes proceeded from the intervascular connective tissue (Axel Key) or from the epithelial covering. The connective tissue around the glomeruli and between the urinary tubules is everywhere enlarged, more markedly in the cortical than in the pyramidal substance. In the dilated interstices we meet with separated bundles of connective tissue, a condition which corresponds to serous infiltration or œdema of the connective tissue. At intervals clusters of red blood-corpuscles are found in the œdematous connective tissue. In some places the connective tissue is granular and abundantly provided with nuclear formations, which is the beginning of interstitial infiltration. The epithelium of the convoluted as well as of the straight, urinary tubules is swollen throughout. Many of the convoluted tubules are enlarged and irregularly sinuous, and their central caliber is reduced to a minimum. In a number of narrow tubules the caliber has entirely disappeared.

The epithelia, especially those of the convoluted tubules, are filled with coarse granules, mostly to such an extent that the nucleus is concealed. This condition, known as "cloudy swelling," is mentioned by all authors, but its nature was unknown. In the acute stage of inflammation we have not to deal with fat granules, which may be proved by simple tests. With high magnifying powers we see that a large majority of the granules within the epithelia are united by fine threads, and such threads we recognize also in the perinuclear rim, wherever the nucleus is visible. Cloudy swelling, therefore, is produced by a growth of the living matter in the epithelia. As I propose to show later, we have here the first steps toward an endogenous production of new elements.

If the acute catarrhal inflammation from its beginning is not severe enough to cause the death of the individual; if, furthermore, it does not affect the entire kidney, but only disseminated foci, either the desquamative or the interstitial form of inflammation is more prominent. I had the opportunity of studying these forms in kidneys of persons who died of tuberculosis, in whom this nephritis is of almost invariable occurrence. (See Fig. 341.)

The calibers of the capillaries are mostly preserved; their walls, however, appear reduced to elements analogous to those which fill the surrounding connective tissue. The glomeruli are moderately enlarged and their vascular loops concealed by abundant, shining, nuclear formations. They present the appearance which Klebs described as "glomerulo-nephritis," a superfluous name in the face of the fact that inflammatory changes of the glomeruli merely accompany the diffuse nephritic process. It seems that in these changes the intra-capsular connective tissue is involved as well as the lining epithelium. Where the tuft is separated from the capsule, or has fallen out, we can convince ourselves that the epithelium of the capsule is for the most part converted into homogeneous, shining lumps, or that the nuclei alone have undergone this change.

The connective tissue between the urinary tubules is widened. Its fibrous structure is retained only in part, while its greatest portion is converted into variously shaped lumps, partly granular and partly homogeneous, representing the so-called "inflammatory infiltration." We see that the majority of the

newly appeared elements are united to each other by fine threads. The membrana propria of the urinary tubules remains intact in this stage of the inflammation.

We find the epithelium in many urinary tubules unchanged or in a condition of cloudy swelling, while numerous convoluted and straight tubules are entirely or partially deprived of their epithelium — the *desquamative nephritis* of authors. Wherever groups of detached epithelia fill the caliber of the urinary tubules, we recognize that the epithelia are smaller and of a more irregular form than normal. We encounter round, angular and spindle-shaped bodies, with and without nuclei, which are, perhaps, newly produced epithelia, detached from the walls of the tubules by a subsequent serous exudation. That a reproduction of epithelia really takes place is indicated by the presence of those peculiar shining bodies which adhere to the otherwise denuded wall.

FIG. 341.—CATARRHAL NEPHRITIS WITH PREVAILING INTERSTITIAL INFLAMMATION.

E, uriniferous tubule, lined with irregular epithelia, *D*, cluster of desquamated epithelia, *L*, shining lumps, from which new formation starts; *I*, considerably broadened interstitial tissue, crowded with inflammatory corpuscles. Magnified 500 diameters.

In the highest degree of catarrhal inflammation, which occurs especially in the cortical substance, in the bundles of straight tubules, all the constituent parts of the kidney-tissue have disappeared in the inflammatory proliferation. (See Fig. 342.) The blood-vessels are no longer recognizable, and not permeable for liquids injected from without. The connective tissue is strewn with shining, homogeneous, irregularly shaped lumps; the membrana propria has disappeared in many places, so that no demarkation is visible between connective tissue and urinary tubules. The latter, especially the narrow tubules, are crowded (as a matter of course, only in places where no desquamation had taken place,) with shining, many-shaped lumps, which are stained a deep red by carmine.

Up to the present time this condition was overlooked by all investigators. The changes consist in the following: In the epithelia, which are often still recognizable by the presence of the irregular caliber of the former tubule, the nuclei or nucleoli, or also single granules, have been converted into shining, irregularly shaped, nearly homogeneous lumps, some of which present distinct partition lines. In some tubules these lumps are present in small numbers, in others they are numerous, and finally the entire epithelium appears converted into such lumps, which are separated from one another by narrow rims of a cement-substance, but are in uninterrupted continuity with each other by means of fine threads. This process is a recurrence of the juvenile condition of living matter. As the same process invades also the connective tissue, the entire structure, especially in the region of the narrow tubules, appears converted into an indifferent or medullary tissue. From this the production of connective tissue proceeds, that leads to cirrhosis and granulation

FIG. 342.—CATARRHAL NEPHRITIS. HIGH DEGREE. TRANSFORMATION OF THE EPITHELIA INTO INDIFFERENT CORPUSCLES.

C, convoluted tubule, lined with epithelium in the stage of "cloudy swelling"; L, remnants of uriniferous tubules, whose epithelia are broken up into homogeneous, shining lumps; I, interstitial tissue, entirely converted into pale granular, or shining indifferent elements. Magnified 500 diameters.

of the kidney. It is this process — formerly incorrectly regarded as entirely interstitial — which results in contraction of the kidney-tissue and in the production of a more or less uniform granulation of the surface. (See Fig. 343.)

If we are to describe concisely the nature of catarrhal inflammation of the kidney we should say that *in the first stage it is characterized by serous transudation into the connective tissue and cloudy swelling of the epithelia; in the second stage, by inflammatory infiltration of the connective tissue, desquamation and reproduction of the epithelium; in the third stage by a metamorphosis of the connective tissue and of the epithelium into an indifferent or medullary tissue.* The inflammation may be of a varying degree of severity; its course may be acute

or subacute; the characteristic feature always is the serous transudation, consequently the absence of casts, a variable percentage of albumen in the urine, and the presence in the urine of tubular epithelia. The inflamed renal tissue at no time ceases to be a tissue, hence, no suppuration occurs. The subsequent course is characterized by destruction of the epithelia amid continuous reproduction of connective tissue, and the final atrophy of the renal tissue, resulting in the formation of the small, contracted, granular, or cirrhotic kidney.

(2) *Croupous (Parenchymatous) Inflammation of the Kidney.* The characteristic feature of croupous inflammation of mucous membranes in general is the presence of a coagulated albuminous substance on the surface, the latter being partially or completely denuded of its epithelium. The inflammation of the connective tissue is always a severe one, betokened by intense redness, swelling, and infiltration with form-elements. Examination with the microscope teaches that the greatest part of the so-called croup-membrane consists

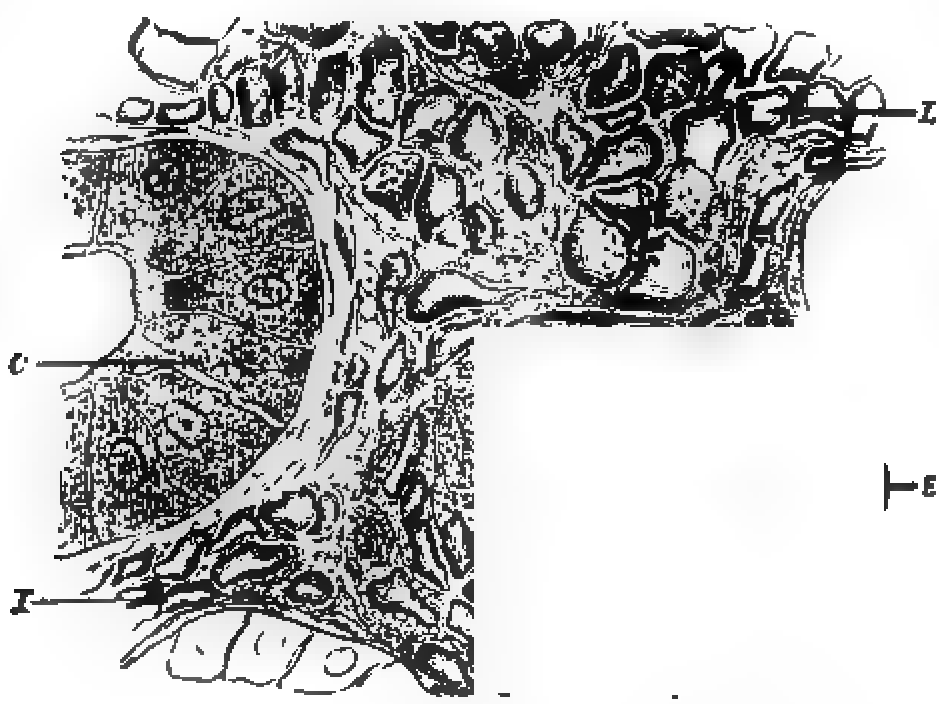

FIG. 343.—CATARRHAL NEPHRITIS. HIGH DEGREE. TRANSFORMATION OF THE EPITHELIA INTO INDIFFERENT CORPUSCLES.

C, convoluted tubule, with coarsely granular epithelia; *E*, remnants of a tubule, without distinct boundary toward the interstitial tissue, the epithelia hold shining, homogeneous lumps; *L*, the epithelia entirely broken up into shining, homogeneous lumps, recurrence of the juvenile condition; *I*, interstitial connective tissue in a similar condition. Magnified 800 diameters.

of a dense net-work of coagulated fibrine, in which varying numbers of bodies of the aspect of nuclei are imbedded. A similar net-work is also invariably found in the air-cells of the lungs in croupous pneumonia, and the absence of coagulated fibrine is regarded as an important feature of catarrhal pneumonia.

The question as to the origin of the croup-membrane has been answered in different ways. Whereas some regard the entire mass as a coagulated exudation from the blood; others (Virchow, E. Wagner) believe it to be a direct product of epithelia, and others again explain the presence of plastids within the croup-membrane by supposing an extensive emigration of colorless blood corpuscles.

If we take into consideration that a fluid exudate before reaching the sur-

face must pass through the walls of the vessels, through the connective tissue intervening between vessels and epithelium, and finally through the epithelia themselves, it is evident that every superficial exudation, before becoming free, must have been an interstitial and a parenchymatous one. The fluid coming from the blood, is taken up by the living epithelia, and may lead to changes such as were described by E. Wagner, but also to the destruction of the epithelia. After the union of the granules of living matter is broken, the granules themselves are imbedded in the coagulating exudate, or are converted into an albuminate no longer viable. This change may occur in the epithelia as well as in the connective tissue after dissolution of the basis-substance. There is nothing to hinder the supposition that with the exudate formed elements of the blood emigrate, and, after being entirely or partially changed, lie imbedded in the now coagulated mass. It is evident that epithelia alone cannot produce a croup-membrane, but require the presence of an exudate from the blood, and the essential constituent of the croup-membrane, under all circumstances, is the coagulable albuminoid body from the blood.

If we apply to the renal tissue the experience gained in other mucous membranes, it follows that the characteristic features of a croupous nephritis, in Traube's sense, consists in the presence of casts. I mean the products known as hyaline and granular casts to which epithelia from the tubules may adhere. The waxy, shining casts may be formations which have undergone secondary changes. These bodies were seen for the first time in 1842 by Henle, and declared to be fibrine. This view was shaken by Rovida,* who stated that the colorless and yellow casts could neither be fibrine, nor gelatine, chondrine, mucine, hyaline, or other colloid substance. Rovida admits, however, that casts possess certain properties of the proteinates which permit their being regarded as derivations of an albuminous substance. According to Axel Key and Ottom. Bayer the casts have arisen from a degeneration of the tubular epithelium and a coalescence of epithelia thus degenerated; both investigators are cognizant of the fact that in tubules which are obstructed by a cast the epithelial lining is present nearly every time and remains intact for a long while. It will scarcely be necessary to go into particulars regarding the secretion theory, since after what has been said the exudation from the blood must under all circumstances pass through the epithelia.

C. Bartels † declares that clinical experience compels him to adhere to the older view concerning the origin of certain forms of casts — namely, that casts are produced by the coagulation of an albuminous substance. This supposition is based on the experience that the presence of casts in the urine depends upon the admixture of albumen with this secretion, since, firstly, such casts are found in the urine in conditions accompanied by albuminuria; and secondly, in the great majority of cases, coincidently with the albumen, casts also appear in the urine. Bartel's views agree with my experience, both clinical and microscopical. I have not seen casts in urine that was free from albumen, but I have quite frequently examined albuminous urine in which casts were not demonstrable. The more abundant the albumen in the urine was, the more certainly could I expect to discover casts, and wherever I had an opportunity to examine kidneys post-mortem which had excreted urine rich in albumen during the life of the patient, and where there had been symptoms of an acute inflammation of the kidney, every time I encountered

* "Ueber das Wesen der Harncylinder. Moleschott's Untersuchungen," XI. Band.
† Ziemssen's "Handbuch der spec. Pathol. und Therap."

a severe degree of inflammatory changes which, on account of the presence of the casts within the tubules, might be called croupous, in the sense of Henle and Traube.

The condition of the kidney of a man, thirty-seven years of age, who died with symptoms of uræmia, on the sixth day after the extirpation of an orbital tumor, is the following: The kidneys increased in size by one-half their bulk, rich in blood, of a doughy softness; the capsule easily stripped; the surface markedly injected; the cortical substance twice as broad as normal; the border toward the pyramids indistinct. The whole tissue, especially that of the cortical substance, of a nearly homogeneous, grayish-red color, evacuating a thick, grayish-red, cloudy fluid when its cut surface is scraped with the knife. The glomeruli appear enlarged, even to the naked eye, and are of a dark red color. Under the microscope the blood-vessels appear dilated, partly filled with blood. The arteries (especially their middle coat), are widened, the muscle-fibers in part coarsely granular, in part converted into homogeneous, shining layers. The glomeruli universally enlarged, their vascular loops dilated, the vascular walls shining and nearly homogeneous; the connective tissue between the loops widened, provided with shining granules and lumps. The capsule and the interstitial connective tissue have for the most part lost their striated character, and appear granular, dotted with numerous, partly homogeneous, partly coarsely granular lumps.

The urinary tubules present changes, as in catarrhal inflammation—the convoluted tubules enlarged and wound; their epithelia in a condition of "cloudy swelling," in part detached from the wall, and lying free in the lumen; in many places the epithelium broken up into yellowish, shining lumps. Moreover, the epithelia of many convoluted and straight tubules present changes which must be regarded as characteristic of croupous inflammation.. The epithelia are swollen up to a complete closure of the lumen; they are converted into globules or plates of a faint luster, which, partly coalescing, represent irregular, caky masses. Finally, all the epithelia of a tubule appear changed into such a mass, in which even the outlines of the former epithelia are recognized; these are the tubular casts. Hyaline or finely granular casts are colorless in the fresh state, and are readily stained by carmine, while, more particularly in the narrow tubules, granular, yellowish plugs occur which do not imbibe the carmine. Since plugs of the latter kind are also to be observed in blood-vessels, nay, even in single loops of the tufts, there can be no doubt that they are albuminates, being essentially the same as the fluid portion of the blood, and stained yellow by the coloring matter of the blood. Wherever the epithelium has gone through the process described, small, shining, spindle-shaped projections are visible on the membrana propria, in part distinctly separated from the caky mass; and where the formation of a hyaline cast is complete, we almost constantly meet with a narrow epithelial layer, composed, in the optical section, of spindles.

Many convoluted tubules contain hyaline casts, the epithelium of the tubules being only slightly changed or desquamated. It is probable that these are casts which have not been formed in situ, but were washed down. Where the cast adheres closely to the wall, the epithelia are either not recognizable, or we see irregular projections of the wall or flat bodies quite irregularly arranged. (See Fig. 344.)

How did the casts originate? Since changes such as described in the epithelia of the uriniferous tubules occur also in the interstitial connective tissue, and even in the blood-vessels, there can be no doubt that the exuda-

tion coming from the blood, if taken up by the tissues in sufficient quantity, and of a certain quality, leads to the swelling up and death of the living matter. The exudation, originally fluid, but coagulated soon after its passage from the vessels, will contain the altered or lifeless part of the tissue. The result of the coagulation is the formation of hyaline or, also, of granular casts in the tubules, and of granular and yellowish hyaline plugs in the blood-vessels and narrow tubules. The casts are products of an albuminous exudation from the blood-vessels, plus the swollen up and destroyed epithelia. This view is supported by the appearance of the vascular loops within the tufts; here the vascular wall is converted into a homogeneous, shining mass,

FIG. 344.—ACUTE CROUPOUS NEPHRITIS.

D, uriniferous tubule, with detached epithelium, *L*, tubule whose epithelium is converted into indifferent elements, *T*, tubule holding a hyaline cast, which probably was washed down from some other part—the epithelium in part desquamated, *I*, interstitial tissue, broadened and crowded with inflammatory corpuscles. Magnified 500 diameters.

which is deeply stained by carmine and exactly corresponds in appearance with the casts.

Under certain circumstances the epithelium of the tubules may partially or totally disappear in the mass which we term tubular cast; but there is always a rapid reproduction starting from those lumps of living matter which adhere to the tubular wall. On the inner coat of the membrana propria we meet with all transitions from yellowish lumps up to the formation of flat epithelia covering the cast.*

* Later observations have led to the conclusion that the flat plastids, which are spindle-shaped in edge-view, are no *epithelia*, but the *endothelia* belonging to the so-called membrana propria of the tubule. With this view the formation of a cast is satisfactorily explained. —ED.

The changes just described I was also enabled to see in the tubules of another kidney, in the immediate neighborhood of small forming abscesses. The circumstance that at times formations resembling nuclei are imbedded in the cast is comprehensible, if we consider that the epithelial body may disappear in the formation of the cast and the nucleus be left unchanged. Granular casts are probably formations in which the epithelia have not yet undergone such extensive changes as are requisite for the production of perfect hyaline casts. Yellow casts are the result of the imbibition of the coloring matter of the blood by the coagulum. Waxy, shining casts may be secondarily changed products, the same as casts which are abundantly provided with fat-granules. (See Fig. 345.)

Not infrequently we observe combinations of catarrhal and croupous nephritis, in which cases abundant desquamated epithelium is to be found in the urine, but only a few hyaline casts. As, according to the above advanced

FIG. 345.—ACUTE CROUPOUS NEPHRITIS IN THE NEIGHBORHOOD OF A FORMING ABSCESS.

C, tubule in transverse section, filled by a hyaline cast; *E*, tubular epithelia at the beginning of proliferation; *I*, interstitial connective tissue crowded with inflammatory corpuscles, their rows probably corresponding with former blood-vessels. Magnified 1000 diameters.

views, all forms of inflammation present only gradual differences, furthermore, even in diffuse nephritis, the kidney is never uniformly diseased throughout its substance, but rather in foci, I believe that the presence of a few casts, especially in the narrow tubules, when accompanied by catarrhal changes in the epithelium of the convoluted tubules, is easily explained. The most numerous blood-vessels run in groups along with the narrow tubules. Here, accordingly, the inflammation can easily reach a higher grade than in the region of the tufts and of the convoluted tubules. This also explains why, after healing of croupous nephritis, irregular cicatricial retractions appear on the surface, between which there are coarse elevations of a comparatively little changed kidney tissue. After croupous nephritis the contraction is always irregular and deep, not leading to a granulation of the surface The large, fatty and amyloid kidneys are probably always products of secondary changes after an original, acute, croupous nephritis.

(3) *Suppurative Inflammation of the Kidney.* The question as to the origin of pus in abscess of the kidney has engaged the attention of several investigators. In 1852, already, George Johnson observed the transformation of the epithelium into pus, especially in the kidney-tissue, notwithstanding his being a strong humoral pathologist. Lipsky * has produced purulent foci in the kidney experimentally, and asserts that the origin of the pus-corpuscles is to be sought for in the epithelium of the uriniferous tubules, by division and by endogenous cell-proliferation.

In considering the fact that the interstitial connective tissue, as well as the epithelium, has abundant living matter, it is plain that in nutritive disturbances the living matter of the tissue in its entirety must undergo changes, and accordingly take part in the process of inflammatory proliferation. Cohnheim's idea that in the inflammatory process an active part is to be ascribed exclusively to the colorless blood-corpuscles, must be regarded a failure.

I have studied the microscopic appearances of suppurative nephritis in the kidney of a man who died with uræmic symptoms caused by hypertrophy of the prostate, which was followed by suppurative cystitis, suppurative pyelitis, and finally, suppurative nephritis. The kidney, especially the cortical substance, had numerous abscesses the size of a millet to that of a hemp-seed.

At some distance from the yellowish pus-foci, which were just recognizable with the naked eye, the blood-vessels, especially the veins, appeared filled to repletion with blood, dilated, while the capillaries only in part have remained recognizable. Many tufts were enlarged and their vascular loops provided with numerous coarsely granular nuclei. The interstitial tissue was partly in the condition of œdematous swelling, partly sprinkled with groups of yellowish, shining lumps. The epithelia appeared in the condition of cloudy swelling; their cement-substance had mostly disappeared, so that many uriniferous tubules were filled with a coarsely granular mass, in which numerous partly homogeneous nuclei were imbedded. Thus, we observe the features of catarrhal nephritis.

In the neighborhood of many purulent foci the picture of a croupous nephritis is presented.† We find most of the uriniferous tubules filled with a hyaline mass, readily stained with carmine; the surrounding epithelial layer in the form of lenticular, flattened-in transverse section spindle-shaped, bodies. The nearer we approach the pus-focus, the more the interstitial tissue appears filled with round, shining lumps, at the same time widened and lacking blood-vessels. The epithelia of the tubules are converted into irregular, shining lumps, or provided with coarse granules, which show marks of division, and, by the manner in which they are grouped, indicate their origin from larger lumps. From the homogeneous lumps up to the coarsely granular nuclear products all intermediate stages may be traced, until all the epithelia appear converted into such nuclear formations, which, in part, lie closely together, in part are separated from each other by granular bioplasson. The membrana propria is still recognizable in this stage, and distinctly marks the tubule from the connective tissue, which frequently contains extravasated red blood-corpuscles, beside similar formations.

Finally, we reach the suppurative focus. (See Fig. 346.) Here the entire

* Wiener Med. Jahrb., 1872.

† Later observations have demonstrated that tuberculosis of the kidney is invariably accompanied by catarrhal nephritis, while suppuration — the production of an abscess — is accompanied by croupous nephritis.—ED.

interstitial tissue is sparsely traversed by unchanged fibers, but mainly converted into a granulated mass, in which only globular, shining, or coarsely granular nuclear bodies, but no isolated elements, are recognizable. The membrana propria is still partly preserved, and we thus ascertain that the epithelium of the tubules has broken up into bodies resembling in every particular those of the connective tissue.

While some suppurative foci are composed principally of homogeneous lumps, which cannot be considered as completed pus-corpuscles, other foci are made up of coarsely granular bioplasson, in which, at nearly equal intervals, nuclei are imbedded. In neither of these cases has a disintegration of the tissue into pus-corpuscles taken place. Foci, on the contrary, which contain fluid pus, already recognizable by the naked eye, under the microscope also present nothing but aggregations of isolated pus-corpuscles. The loops of the tufts also take part in the production of pus, inasmuch as the walls of

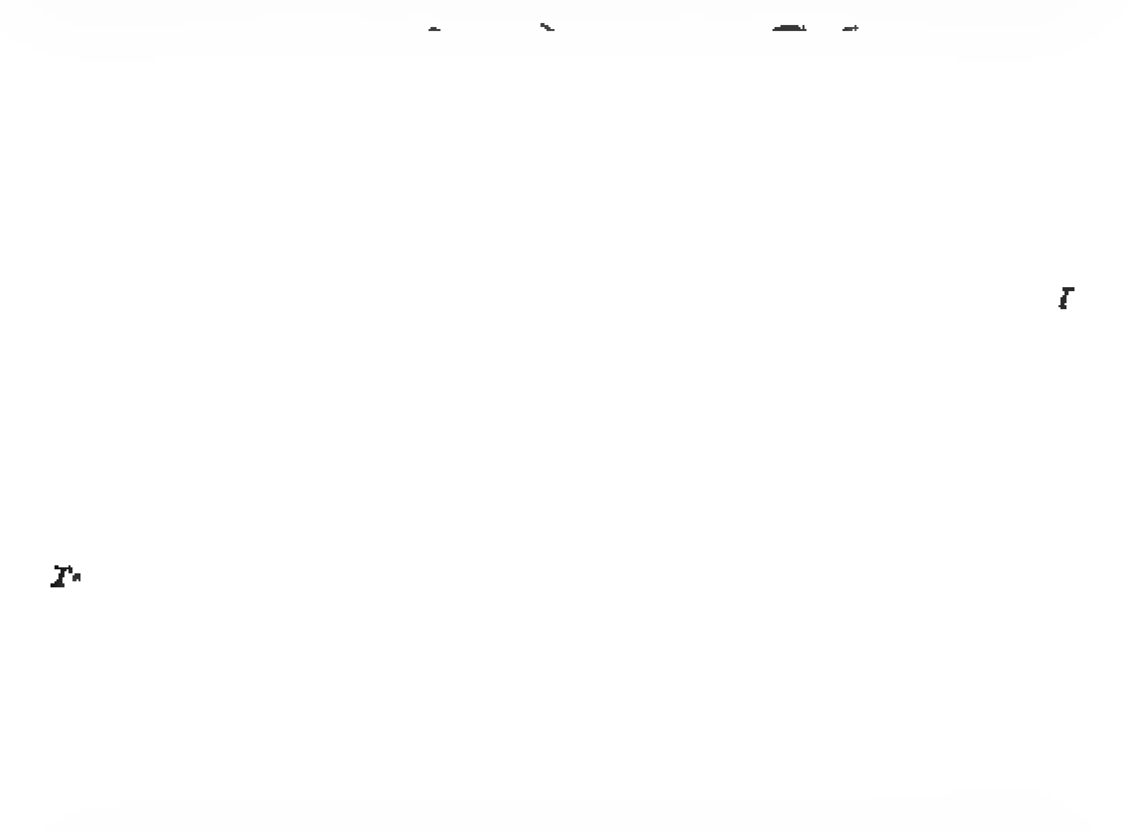

Fig. 346.—Suppurative Nephritis.

T, remnants of uriniferous tubules, whose epithelia are coalesced into multinuclear masses, their boundary line in part destroyed by the inflammatory infiltration, *I*, interstitial tissue, almost completely converted into inflammatory corpuscles, all blood-vessels destroyed. The breaking-up into single pus-corpuscles not yet accomplished. Magnified 500 diameters.

the vessels at first split into shining lumps and subsequently into pus-corpuscles.

The course of suppuration is, therefore, the following: In the first place, it is clear that interstitial tissue, as well as epithelium, can be converted into pus; the living matter of either of these tissues may return to the juvenile state, the granules becoming enlarged, homogeneous, and shining. We notice groups of such lumps scattered throughout the interstitial and the epithelial tissue. (See Fig. 347.)

Next, with an increasing number of these lumps, the tissue *in toto* appears converted into a conglomerate of shining lumps, and finally, a differentiation into nucleated corpuscles takes place, representing a stage in which the former tissue is still a tissue, though markedly altered. Only when the continuous mass is torn into separate, nucleated lumps have we to deal with finished pus. The tissue is destroyed — in its place we have an abscess.

The endogenous proliferation of living matter takes place in exactly the same manner in connective tissue and in epithelium. The division into single elements is always a secondary process, and can occur in every stage of the proliferation. Homogeneous lumps break up into a number of granules by the formation of new lines of division within the lump. In the beginning every lump and every granule is united to all its neighbors by fine threads. The living connection is retained even after nucleated bodies have formed from the lumps; the connection is broken after the formation of pus-corpuscles.

L

FIG. 347.—SUPPURATIVE NEPHRITIS.

C, uriniferous tubule, filled with a cast, in which remnants of nuclei are imbedded; *L*, tubular epithelium, in active new formation of living matter, in the early stages of endogenous formation of pus-corpuscles; *V*, red blood-corpuscles, partly in vessels, partly extravasated in the interstitial tissue, which holds a number of coarsely granular corpuscles. Magnified 800 diameters.

CHRONIC INFLAMMATION OF THE KIDNEYS. BY JEANNETTE B. GREENE, M. D.*

In accordance with the plan pursued in the laboratory of C. Heitzmann for the last seven years, we divide chronic nephritis into three main varieties, namely, the *catarrhal*, the *croupous*, and the *suppurative*. All these varieties of nephritis may appear in the acute form also. Chronic catarrhal, and croupous nephritis may be accompanied by acute recurrences of the disease, and in this way give rise to a secondary subacute condition.

It is unnecessary to say that such terms as "catarrhal" and "croupous" have no special significance; but, after having been once adopted in our

* Printed from the author's manuscript.

nomenclature, they may be preserved, and certainly are to be preferred to such expressions as "interstitial," "desquamative," or "parenchymatous" nephritis, which were introduced by Virchow. In nephritis, as in every inflammation, the morbid process starts from the vascularized connective tissue, while the participation of the epithelia is only secondary. Every form of nephritis must, therefore, from necessity, be interstitial and parenchymatous at the same time.

The term "Bright's disease," I think, ought not to be employed by any scientific person, for it has no significance, and the group of morbid phenomena considered under that head include both the primary and secondary changes of the kidney-tissue.

(1) *Chronic Catarrhal Nephritis.* We know that in certain forms of nephritis the urine contains no albumen, or very little, which may, however, be temporarily increased; that it contains kidney epithelia detached from the convoluted and the straight tubules, pus- and blood-corpuscles, and occasionally a hyaline cast, usually from the narrow tubes. The clinical features of the disease are widely different in different individuals. In cases of this kind death may ensue and the kidneys exhibit the appearances described in the preceding article. Should the disease, on the contrary, be prolonged for several months or years, the result of this chronic action is found to be a shrinkage of all the kidney-tissues, and this condition is briefly termed *cirrhosis*. *Chronic catarrhal nephritis and cirrhosis are therefore identical.*

In the milder forms of this disease the surface of the kidney is irregularly, though slightly retracted. The capsule is in most cases adherent and follows the inequalities of the retractions. The diameters of both the cortical and pyramidal substances are somewhat decreased, and all parts of the kidney show, even to the naked eye, grayish radiating striæ. Under the microscope, with low powers the striæ prove to be newly formed connective tissue, which is most abundant in the medullary rays of both the cortex and the pyramids, and it is the retraction of this newly formed tissue which causes the irregularities of the surface. In the more severe forms of chronic catarrhal nephritis the whole kidney is considerably reduced in size and the inequalities on the surface are very decidedly marked. In transverse section both the cortical and pyramidal substances are seen to be much narrower than in the normal condition. This is more particularly the case in the cortex, of which, in more advanced degrees, only slight remnants are left, and these correspond with the elevations of the surface. It is further observed under the microscope that the newly formed connective tissue is most developed corresponding with the medullary rays, between the straight, narrow tubules, which are reduced in number. Injected specimens of cirrhotic kidneys show plainly a deficiency of blood-vessels in the medullary rays of both the cortex and pyramids. The capillary reticulum around the tufts and tubules is also scanty. The calibers of the capillaries are in many places irregularly distended, and the vasa recta, which are capillary prolongations extending into the pyramidal substance, are narrower than the normal vessels. At the points of transition of cortical capillaries into vasa recta, the difference in their respective calibers is less marked than in the normal kidney.

The question now arises, What are the changes which take place in the kidney-tissue, producing destruction of tufts, tubules, and blood-vessels, and giving rise to such an extensive new formation of connective tissue in their stead?

I am able to corroborate the statement made by A. Meyer, that in the process of catarrhal nephritis in the cortical substance many tubules are destroyed, and that their epithelia, after a considerable increase of living matter, break down into medullary corpuscles, from which a new formation of connective tissue subsequently arises. This destructive process in chronic catarrhal nephritis invades first — and in the highest degree — the narrow tubules running in the medullary rays. By a swelling of the epithelia the calibers of the tubules are obliterated, the epithelia then break down and form rows of medullary corpuscles. A corresponding change takes place in the capillary blood-vessels in the neighborhood. These metamorphoses result in the formation of a tissue, which, from the presence of basis-substance, must be regarded as connective tissue, though it rarely becomes fibrous, and the vascular supply is always scanty. If a number of tubules in the medullary rays are involved in this destructive process, the surface of the kidney corresponding to them will be retracted by the cicatricial tissue.

The obliteration of a number of the narrow tubules, including the ascending and descending branches, would explain the clinical fact that persons affected with cirrhosis void large quantities of urine almost destitute of salts. We know, from the results of Bowman's investigations, which have recently been corroborated by R. Heidenhain, that the tuft excretes water only, and this becomes thicker by the addition of the saline constituents excreted by the narrow tubules. It is in the narrow tubules that much of the watery part of the urine is restored to the thickened blood which runs in the neighboring capillaries, including also the vasa recta of the pyramids. If the function of the tubules be much interfered with, the interchange between the liquid contents of the tubes and the solid constituents of the blood will not take place, and consequently the urine will be voided in about the same condition in which it was pressed into the capsule from the tuft. Numbers of the convoluted tubules perish also through the increased formation of connective tissue, while from others the epithelia are simply desquamated, and, together with pus-corpuscles, which are the offspring of epithelia, appear in the urine. Both the quantity and the character of the urine, as well as its morphological elements visible under the microscope, enable us with certainty to make a diagnosis of cirrhosis of the kidney.

From the above description it is evident that interstitial and desquamative nephritis are concomitant features of chronic catarrhal nephritis, and that the latter expression includes the two former.

In high degrees of cirrhosis many of the tufts are completely destroyed. I have been able to trace the changes by which the destruction is brought about. At first the tuft appears slightly enlarged and crowded with bodies having the appearance of nuclei, and which undoubtedly originated from the covering epithelia and from the endothelia of the capillary walls. By this process the calibers of the vessels are obliterated, and all that remains of the former capillaries is a solid cord. Next the solidified capillaries break down into medullary or inflammatory corpuscles, and in this stage the tuft consists of an aggregation of inflammatory corpuscles. The capsule is usually considerably thickened, and between it and the inflammatory bodies no space can be recognized. In the succeeding stage the medullary corpuscles are transformed into homogeneous or faintly striated connective tissue containing only a very limited number of plastids.

After passing through these changes the tuft is reduced to a half or a third of its original size. The capillaries remain only as radiating strings, and these, with the altered capsule, admit the diagnosis of an atrophied and solidified tuft, which is often found to be in waxy degeneration. Sometimes around the atrophied tuft, consisting of a solid mass of connective tissue, a light space is observed, traversed by delicate fibers and remnants of the epithelia of the tuft and the capsule. This is a newly formed, probably myxomatous basis-substance, which is produced by medullary corpuscles, the offspring of the glomerular epithelia. (See Fig. 348.)

In a more acute course of the disease, the tuft, together with the capsule and all the surrounding tissues, including interstitial connective tissue, blood-vessels, and convoluted tubules, break down into a mass of inflammatory corpuscles, resulting in an extensive new formation of connective tissue, or a

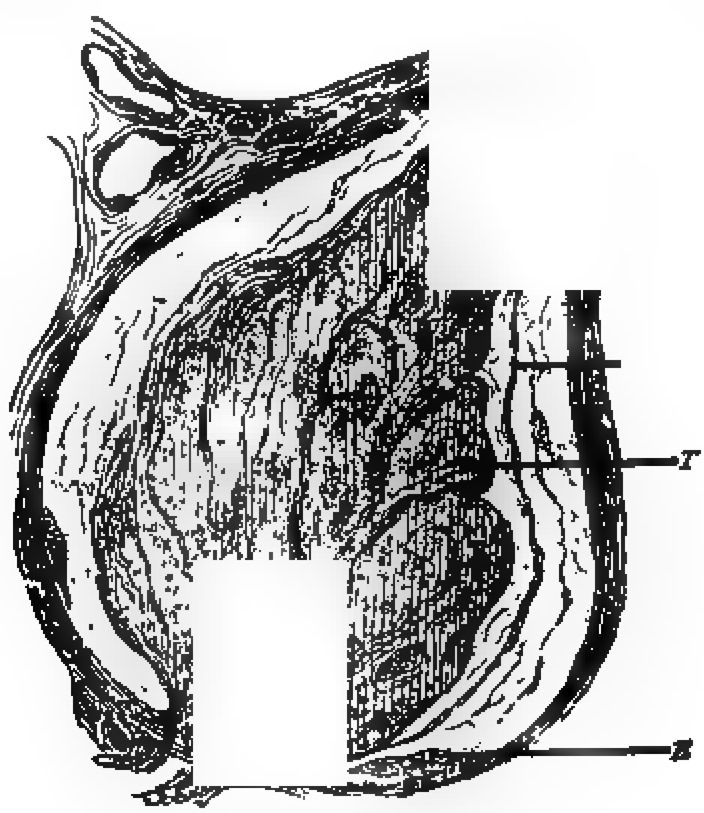

FIG. 348.—CIRRHOSIS OF THE KIDNEY. ATROPHIED TUFT.

T, tuft, transformed into fibrous connective tissue. *R*, remnants of epithelia of the tuft. *S*, structureless, newly formed basis-substance; *E*, remnants of epithelia of the capsule. *C*, considerably thickened capsule. Magnified 500 diameters.

formation of cysts. Apparently an already atrophied tuft may in an acute recurrence of nephritis break down into inflammatory corpuscles, and at last disappear entirely. From this description it is evident that the term "glomerulo-nephritis," introduced by Klebs, is superfluous, for the inflammatory changes of the tuft are invariably connected with general nephritis.

I have also made examination of the changes which, in chronic catarrhal nephritis, take place in the arterial coats, and which result in the destruction of even large arterial vessels. (See Fig. 349.)

The first thing noticed is that the lining endothelia of the artery are enlarged and coarsely granular, and that a proliferation of inflammatory corpus-

cles takes place, encroaching upon the caliber, rendering it irregular, as if compressed. Often, however, the narrowed lumen contains a finely granular or homogeneous mass, probably plasma of the blood. The spindles of the smooth muscle-fibers of the middle coat are transformed into inflammatory corpuscles. These bodies, at first, are not numerous, but, in more advanced stages, appear to compose the entire tissue, which still preserves a resemblance to the original smooth muscle-structure. These characteristics are particularly well marked in transverse sections, where a decided increase in the circumference of the vessels is also noticed. Similar changes take place in the external coat, till finally the entire arterial wall is converted into a solid connective-tissue cord, which may, in places, still show faint traces of the former caliber. Cords of this kind, as a general thing, present the features of waxy degeneration.

(2) *Chronic Croupous Nephritis.* The clinical features of this form of nephritis are somewhat different from those attending cirrhosis.

FIG. 349.—CIRRHOSIS OF KIDNEY. INFLAMMATION OF AN ARTERY.

E, endothelia in active proliferation, the caliber considerably narrowed; *M*, middle coat, the smooth muscles in part transformed into rows of inflammatory corpuscles; *A*, adventitial coat, crowded with inflammatory corpuscles, partly sprung from the capillaries of the adventitia. Magnified 600 diameters.

In chronic croupous nephritis symptoms of uræmia are more common than in the cirrhotic form, and sudden death is much more frequent. The urine invariably contains casts and albumen; the former are usually granular, and waxy or fatty if the corresponding changes have taken place in the diseased kidney. Hyaline, epithelial, and blood casts may also appear in addition to those first enumerated, if an acute attack of inflammation is superadded to

the existing chronic affection. In persons dead of chronic croupous nephritis of long standing, the kidney is found to have an entirely different appearance from the cirrhotic kidney. It is more frequently enlarged than diminished in size. The surface is often nodulated, and between the nodules are seen deep cicatricial retractions. These retractions are never found uniformly over the surface. The capsule is adherent to the retractions. In transverse sections of a kidney of this kind we find that the cortical substance is absent in those parts corresponding with the retractions of the surface, while in other places the cortex may be unaltered, or even increased in bulk. The pyramidal substance may be unchanged, or it may be diminished. In contradistinction to the more or less uniform shrinkage of the kidney—called cirrhotic—the partial destruction of the tissue which occurs in chronic croupous nephritis might be designated *atrophy;* for, under the microscope, we find in the most diseased portions only traces of the original kidney structure.

Cysts are found to be larger and more numerous in kidneys affected with chronic croupous nephritis than in those which are contracted and reduced by cirrhosis. Both fatty and waxy degeneration are met with in cirrhotic as well as in atrophied kidneys, but these changes are more extensive in the latter than in the former. In the so-called "large, white kidney" the highest degrees of fatty degeneration occur as a secondary result of chronic croupous nephritis. The "lardaceous" change is also a secondary condition of this form of nephritis.

In sections of the depressed cicatricial portions of the cortical substance of kidneys in chronic croupous nephritis, we find a large amount of connective tissue, which may be either homogeneous or fibrous, and which has only a scanty supply of blood-vessels. In the cirrhotic kidney the newly formed connective tissue is more or less regularly distributed throughout the kidney structure. The uriniferous tubules are in part transformed into connective tissue, while still retaining the outlines of their original configuration. In atrophy of kidney, on the contrary, there is no regularity in the arrangement of the connective tissue, and we find only remnants of the former tubules. We further observe in these latter cases irregularly scattered sections of tubules, from which the epithelial lining has entirely disappeared. Other tubules, still recognizable by their shape, are crowded with inflammatory bodies, which have evidently arisen from the tubular epithelia in the formative stage of connective tissue. The connective tissue, more particularly in the subacute forms of croupous nephritis, is often observed to be filled with inflammatory corpuscles; and in the midst of groups of these bodies of the ordinary color, and readily taking the carmine stain, we also find aggregations of corpuscles, light brown in color, and unaffected by the carmine. I am inclined to regard these formations as the offspring of the former epithelia of the tubules. (See Fig. 350.)

Not infrequently, in the middle of these brownish clusters, hyaline casts may be found; these probably originated in the convoluted tubules of the first order, and were too large to be carried through the narrow tubules. What the ultimate fate of these casts may be, we can only surmise. The tufts, as in cirrhosis, are reduced to a mass of medullary corpuscles, and a similar change takes place in the surrounding capsule. These facts lead to the conclusion that a destruction of the epithelial and vascular structures takes place, with the final result of a new formation of connective tissue.

In the highest degrees of chronic croupous nephritis, in addition to the

atrophied portions we find districts where a considerable amount of connective tissue has developed, thus constituting a true *hypertrophy*, or *hyperplasia*. This tissue surrounds the tubules, which in a majority of cases are entirely without epithelia. The epithelia may have been carried away by simple desquamation, or have perished in the formation of casts. In many of the narrow tubules, from which the epithelia have disappeared, we find a row of narrow endothelia, detached in places from the connective-tissue wall. A kidney of the above description may with as much propriety be called hypertrophied as a lung or a glandular organ in a like condition. (See Fig. 351.)

Concerning the formation of casts, my observations convince me that the epithelia lining the tubule, becoming saturated with the albuminous exudate, swell, grow pale, and finally produce the mass called a tubular cast. In many cases the cast has the appearance of having been constructed of a number of hyaline or granular lumps resembling former epithelia. Around the cast, at

FIG. 350.—ATROPHY OF KIDNEY, AFTER CROUPOUS NEPHRITIS.

C, indistinctly fibrous connective tissue, *I*, cluster of medullary corpuscles, sprung from former tubular epithelia, *T*, tubule, deprived of its epithelia; *H*, tubule, containing a granular cast. Magnified 600 diameters.

its place of origin, we almost invariably see a wreath of endothelia lying between it and the wall of the tube, indicating that after the formation of the cast a reproduction of endothelia had taken place, or that they had been brought into view by the liquefaction of the hyaline, so-called basement-membrane. The presence of this endothelial wreath seems to be satisfactory proof that the cast was formed in the situation where we find it. If a cast is seen not quite filling the caliber of the tubule which is still lined with unchanged epithelia, the most reasonable presumption is that it has been transported to its present locality from a narrower part of the uriniferous

tubule, where it must have originated. The same may be said of casts found in tubules entirely stripped of epithelia, whose calibers are broader than the diameters of the casts. It cannot be denied that a mass closely resembling a hyaline cast may be produced from endothelia; for I have seen such irregular formations lying along the border of a tubule bounded toward the center of the caliber by a row of epithelia, which had been detached by the exudate and undergone no change. Formations of this kind are, however, very exceptional.

In chronic croupous nephritis granular casts are commonly found to be more abundant than other varieties, the granules being probably due to a disintegration of the ensheathing endothelia. Fatty and waxy casts are also

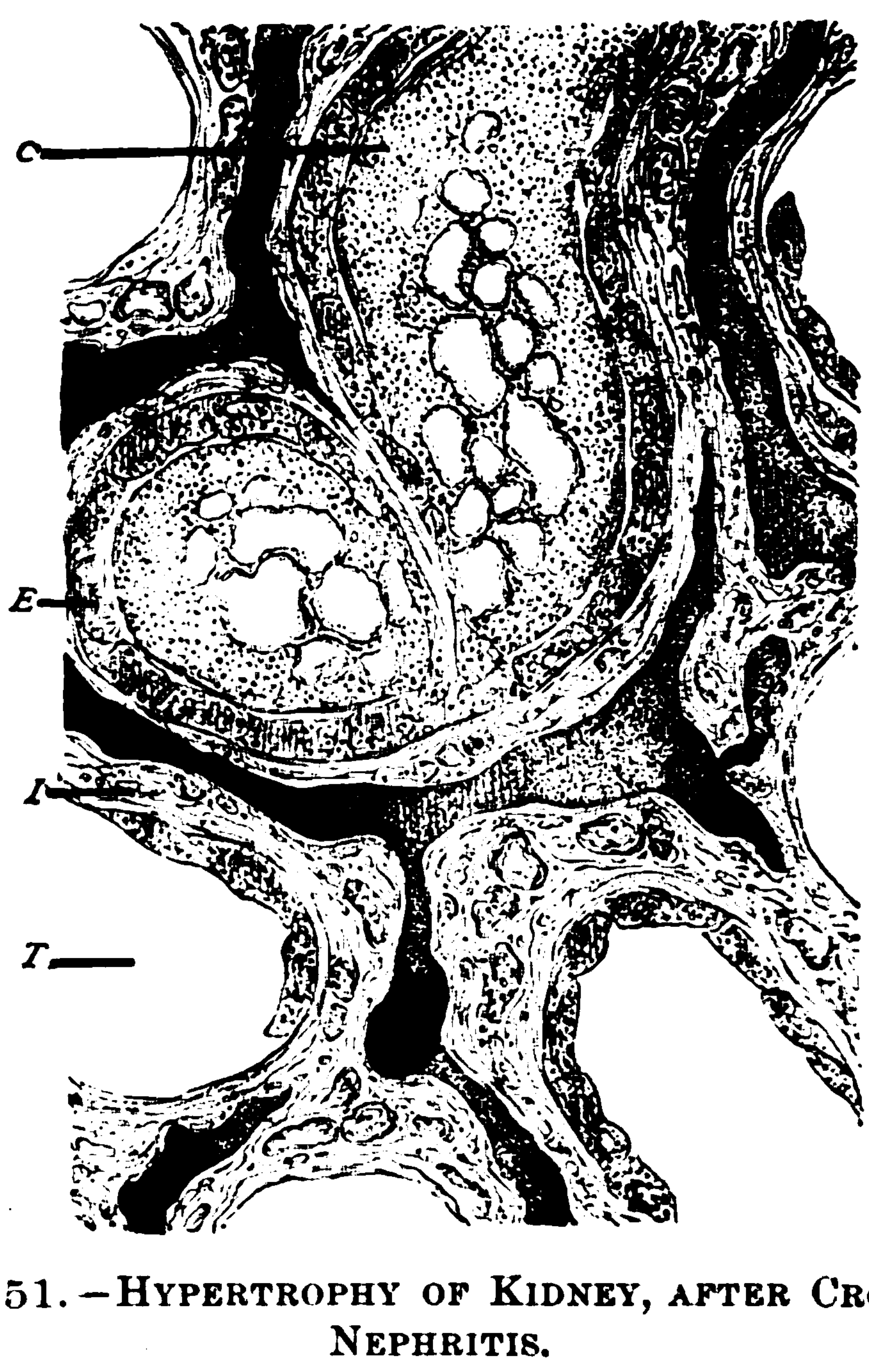

FIG. 351.—HYPERTROPHY OF KIDNEY, AFTER CROUPOUS NEPHRITIS.

C, granular cast, holding in its center waxy lumps; *E*, endothelial lining of the tubule around the cast; *T*, empty tubule; *I*, interstitial connective tissue, with injected blood-vessels, holding a moderate number of inflammatory corpuscles. Magnified 600 diameters.

features of this form of nephritis; these always indicate a similar metamorphosis in the kidney-tissue itself.

(3) In *chronic suppurative nephritis* abscesses formed in the kidney may exceptionally lead to the production of a dense connective-tissue capsule—the "pyogenous membrane" of writers—and pus, under these conditions, becomes inspissated into a cheesy mass, which, by some, has been mistaken for tubercle.

A formation of this kind may be termed a *chronic abscess* of the kidney,

and has nothing in common with tubercle, except that, the watery portions having been absorbed, the pus-corpuscles shrivel and become partly transformed into fat-granules. In the caseous and fatty degenerations of tubercle we observe an analogous result, the cause of these processes being identical —*i. e.*, the absence of blood-vessels.

Formation of Cysts. Pathologists hold widely differing views regarding the origin of cysts. Some claim that cysts arise from the distended capsules, entirely overlooking the fact that cysts are not infrequently found at the periphery of the kidney, where there are no tufts. Others believe that cysts start in an expanded tubule, without attempting to explain the process by which the tubule attains the size of a cyst.

I have frequently observed tufts which were considerably reduced in size, while the space between them and the wall of the capsule was filled with a finely granular mass, evidently sero-albuminous in nature. The capsule was in no instance markedly distended, its diameter not noticeably exceeding that of the normal capsular space. Probably such a condition arose from a choking of the uriniferous tubule, followed by a damming back into the capsule of

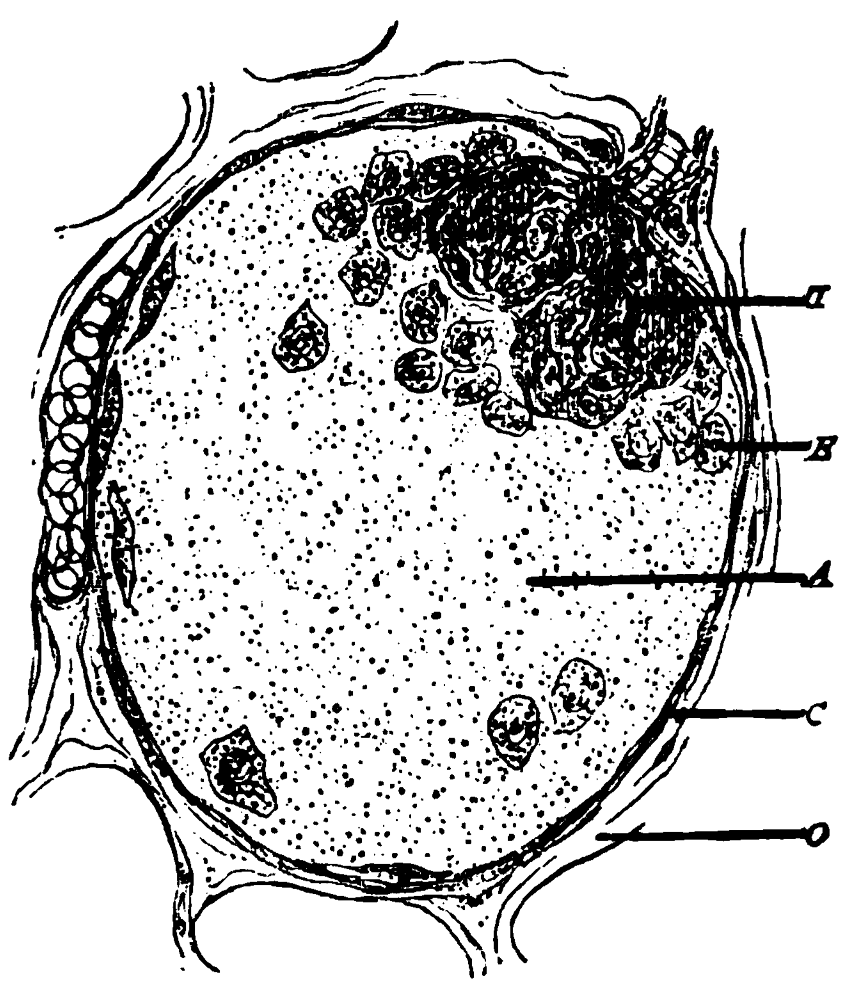

FIG. 352.—COMPRESSED TUFT IN A CAPSULE, FILLED WITH SERO-ALBUMINOUS LIQUID. CIRRHOTIC KIDNEY.

T, compressed tuft; *E*, detached epithelia of the tuft; *A*, finely granular, sero-albuminous liquid; *C*, capsule of tuft, unchanged; *O*, interstitial, slightly œdematous connective tissue. Magnified 500 diameters.

the liquid excreted by the tuft. In consequence of the pressure of the accumulated liquid the tuft was compressed more and more, until finally its function was abolished. I doubt if we have any good reason for terming such formations cysts. (See Fig. 352.)

A more satisfactory explanation of the production of cysts is the following: The first thing noticed is an abundant formation of inflammatory corpuscles in circumscribed districts of the kidney-tissue. These may be situated in the cortex or in the pyramidal substance. Many of these corpuscles evi-

dently originated from tubular epithelia. The second stage is characterized by the swelling of the inflammatory bodies, which afterward become pale, and, by a process of liquefaction or mucoid degeneration, are transformed into a hyaline, apparently structureless, mass. We very frequently find in this mass delicate granular fibers, which resemble those of myxomatous tissue. The new formation thus produced may, at the outset, be extremely small and irregularly bounded by unchanged medullary corpuscles. With the growth of the cyst more medullary bodies gradually become liquefied, till at length a cavity is established, containing a sero-albuminous fluid, and bounded by flattened, polyhedral medullary corpuscles, which, in this situation, might be designated endothelia. At the periphery a formation of fibrous basis-substance takes place, with the production of a cap-

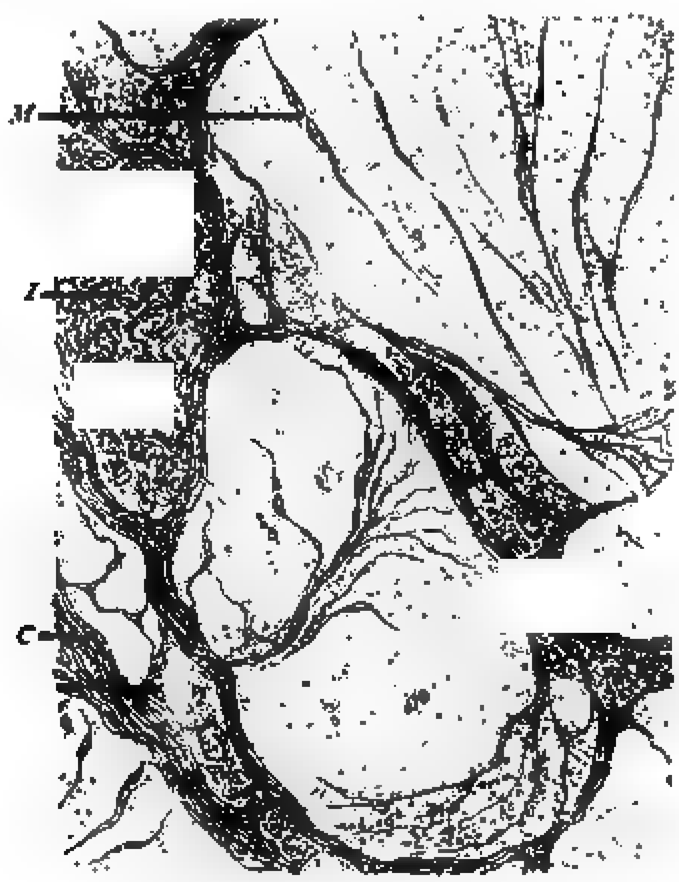

FIG. 353.—CYSTIC DEGENERATION OF THE KIDNEY IN CHRONIC CROUPOUS NEPHRITIS.

I, mass of inflammatory corpuscles; *M*, strings of a myxomatous connective tissue traversing cystic spaces, which are filled with a sero-albuminous liquid; *C*, fibrous connective tissue producing the wall of the cysts. Magnified 600 diameters.

sule—the cyst-wall proper. Cysts, therefore, are the products of secondary changes of medullary bodies which had their origin in kidney epithelia. (See Fig. 353.)

Fatty Degeneration. In all forms of chronic nephritis fat may appear in any of the constituent tissues of the kidney; more especially, however, in the epithelia and in the interstitial connective tissue. Fat-granules unquestionably originate from particles of living matter, for in the epithelia we are able to recognize their connection by delicate filaments with the bioplasson reticulum.

In the connective tissue fat-granules are often observed in the basis-substance, thus proving that the basis-substance is pervaded by living matter. In high degrees of fatty metamorphosis, which are observed in cirrhotic as well as in atrophied and hypertrophied kidneys after chronic croupous nephritis, the fat-granules coalesce and form globules which to a great extent replace the epithelia of the tubules. Large fat-globules are also found in the interstitial connective tissue, which is under these circumstances always increased in bulk. (See Fig. 354.)

Fatty casts, in all probability, originate from a disintegration of the endothelia, which had previously undergone a high degree of fatty change. In the same way can be explained the presence of the large amount of fat-granules and globules sometimes observed in the urine. This condition is always a satisfactory proof that a high degree of fatty degeneration has taken place in the kidneys.

Waxy Degeneration. The epithelia of the tubules which have, in a measure, escaped the inflammatory action, may become the seat of waxy degeneration, when a similar condition has reached an advanced stage throughout the

FIG. 354.—FATTY DEGENERATION OF THE KIDNEY IN CHRONIC CROUPOUS NEPHRITIS.

E, tubular epithelia, containing granules and globules of fat, *F*, fat-globules in the widened interstitial connective tissue, *B*, capillary blood-vessel. Magnified 600 diameters.

kidney-tissue. These epithelia sometimes assume the appearance of large, glistening bodies projecting irregularly toward the center of the caliber of the tube. When desquamated they are seen in the urine as more or less shining, homogeneous bodies, and readily recognized as waxy.

In chronic croupous nephritis, waxy casts are sometimes observed studded with waxy epithelia, or with granules, producing the epithelial or granular waxy casts. The formations of waxy casts in the tubules may be easily traced from the epithelia, which are changed into waxy globules, in part homogeneous and in part granular, and which by coalescence evidently form waxy casts. Around these casts a wreath of endothelia, also in waxy degeneration, may be recognized. (See Fig. 355.)

I have often found the connective tissue, both in chronic catarrhal and in chronic croupous nephritis, the seat of waxy degeneration, but, as before stated, the highest degrees of this change are unquestionably observed in chronic croupous nephritis. Simultaneously with the changes above described, the walls of the blood-vessels in the connective tissue also undergo waxy degeneration. I have occasionally seen specimens in which the capillary coat was broadened and exhibited marked signs of waxy degeneration, even before the arterial walls were affected. The more common occurrence, however, is for the middle coat of the artery to give the first indications of the invasion of this metamorphosis, a characteristic which is the rule in waxy degeneration of the spleen.

The tufts are also very frequently involved in the waxy metamorphosis, and I have hardly seen a case of atrophy or cirrhosis without a waxy change

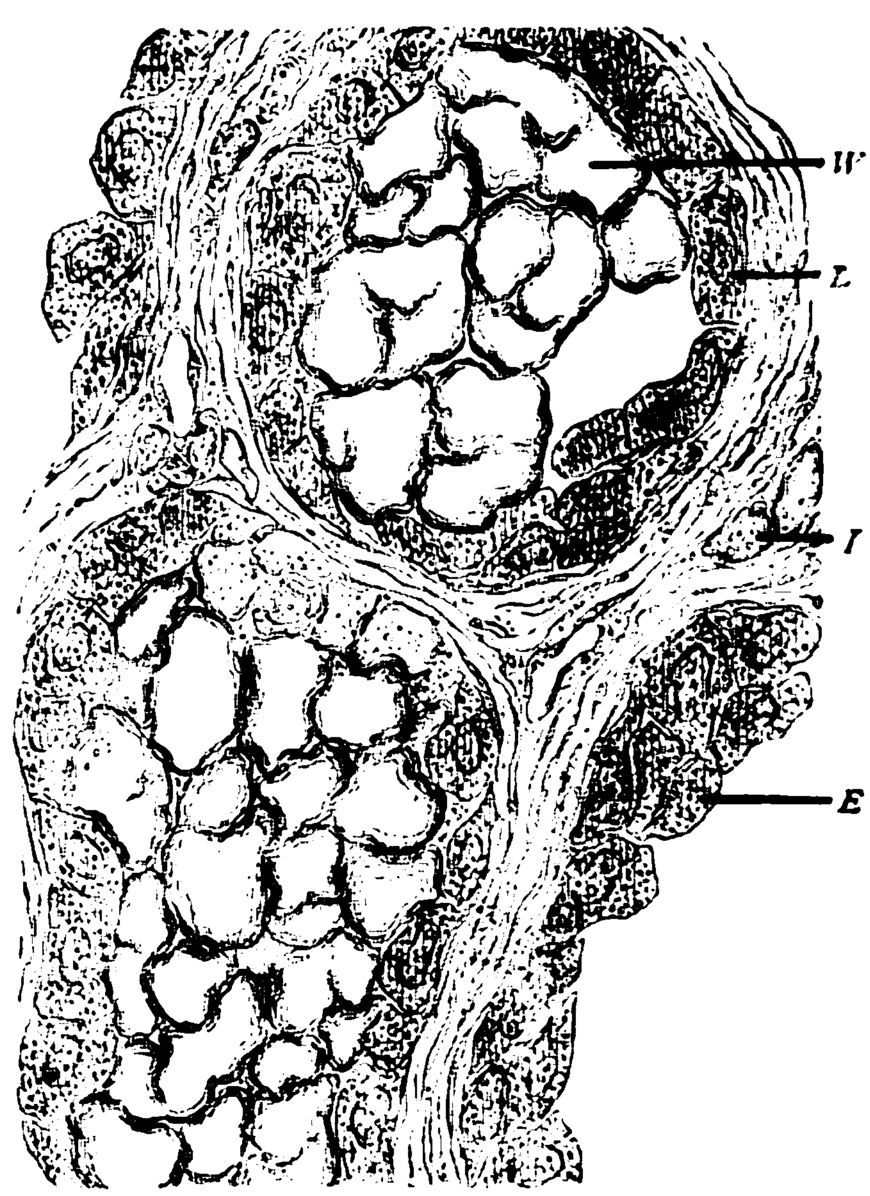

FIG. 355.—WAXY DEGENERATION OF THE KIDNEY IN CHRONIC CROUPOUS NEPHRITIS; FORMATION OF A WAXY CAST.

W, shining, waxy lumps in the caliber of the tubule; *L*, epithelia and endothelia of the tubule, partly in waxy change; *E*, unchanged tubular epithelia; *I*, interstitial connective tissue. Magnified 600 diameters.

of the tufts more or less marked. The tuft may, at the same time, be considerably enlarged, or it may show no increase in size. It is far more common, however, to find the tuft atrophied and solidified, the calibers of the capillary vessels obliterated, when invaded by the waxy degeneration.

I have occasionally noticed in the veins, clots which were composed of highly refracting globules, some of which exceeded the size of red blood-corpuscles, each showing a central depression, and suggesting the idea that

wavy degeneration of the red corpuscles had taken place. In the connective tissue I have seen, though very rarely, clusters presenting the appearance above described, which, perhaps, might be considered waxy degeneration of extravasated blood.

In the course of my researches I studied sixteen kidneys, five of which were affected with chronic catarrhal nephritis, and eleven with chronic croupous nephritis, and the conclusions arrived at were the following:

First. Chronic catarrhal nephritis induces a new formation of connective tissue throughout the kidney, which tissue is formed at the expense of the uriniferous tubules. The surface of the kidney is marked by shallow depressions, or by granulations, more or less uniformly distributed. Chronic catarrhal nephritis invariably leads to a shrinkage of the kidney — cirrhosis.

Second. Chronic croupous nephritis may result in atrophy of circumscribed portions of the kidney, with more or less destruction of the epithelial formations of the affected parts. The surface of the kidney shows deep retractions, between which the cortical substance remains comparatively unchanged. Chronic croupous nephritis may also terminate in hypertrophy of the kidney, with an increase of its bulk. This increase is due to an augmentation of the interstitial connective tissue, which, as a rule, is accompanied by a narrowing of the tubules, and an almost complete destruction and desquamation of the epithelia.

Third. Suppurative nephritis may become chronic with an encapsulation of the abscess, followed by a caseous metamorphosis of the pus.

Fourth. Cystic degeneration may occur both in chronic catarrhal and chronic croupous nephritis. Cysts are formed by a mucoid degeneration and liquefaction of inflammatory corpuscles which are the products of former epithelial bodies. In the early stages of cyst-formation the cavity is traversed by myxomatous tissue and irregularly bounded by inflammatory corpuscles. In completed cysts a sero-albuminous liquid is found, and the capsule is lined by a layer of flat endothelia. Neither the capsule of the tuft nor the uriniferous tubules participate directly in the formation of cysts.

Fifth. Fatty degeneration occurs both in chronic catarrhal and chronic croupous nephritis, reaching the highest degree, however, in the latter form of disease. It consists of a transformation of bioplasson-granules into fat-granules both within the epithelia and in the connective tissue. In high degrees of degenerative change the fat-granules fuse together and form globules, which are often arranged in clusters.

Sixth. Waxy degeneration is a feature common to all forms of chronic nephritis. It invades the epithelia and ultimately produces waxy casts. In many instances, connective tissue, capillaries, tufts, and arteries are all involved in the process. Atrophied tufts are almost invariably the seat of waxy degeneration.

(2) The *calices, the pelvis, and the ureter* are constructed after the manner of all mucous membranes. The most internal layer is fibrous connective tissue, covered by stratified epithelia; the middle layers are composed of smooth muscle-fibers, and the outermost layer is of loose, fibrous connective tissue. The mucosa is made up of dense connective tissue, immediately below the epithelial lining, and of delicate, loose connective tissue close above the muscle-layers. The latter arrangement allows the for-

mation of large folds of the mucosa, which occlude the caliber of all the above-named hollow formations when at rest. The covering epithelium is stratified, and composed of a limited amount of the columnar, cuboidal, and flat varieties, the latter having often a caudate appearance—*i. e.*, supplied with a number of offshoots penetrating between the epithelia of the next deeper layer. Racemose, mucous glands are said to occur in the mucosa of the pelvis, but are absent from the mucosa of the ureter. (See Fig. 356.)

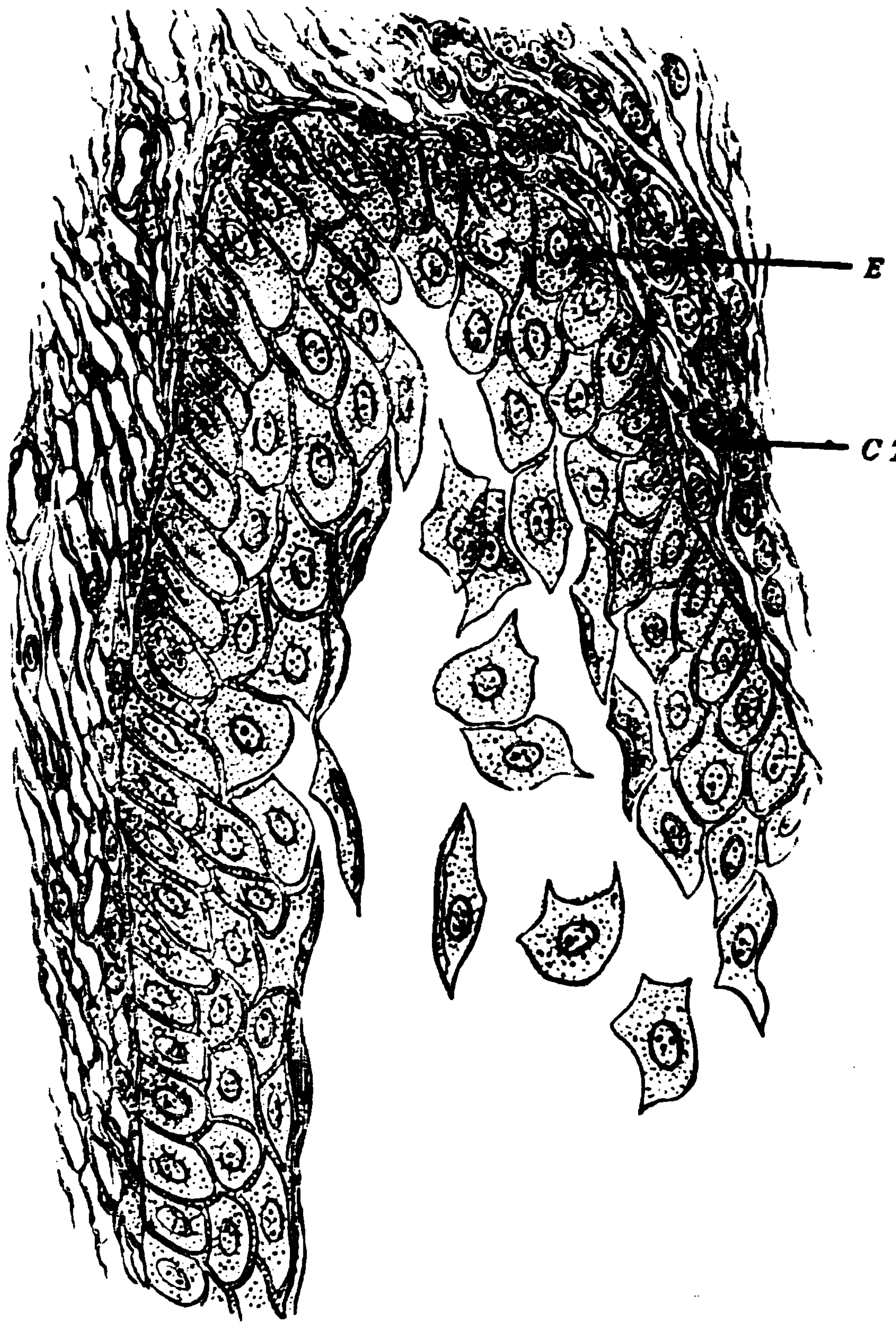

FIG. 356.—CALYX OF THE KIDNEY OF A DOG.

E, stratified epithelia; *CT*, connective tissue. Magnified 600 diameters.

The muscle produces at least two layers—an inner longitudinal, which is most developed, and an outer circular layer. The circular muscle-fibers are the only ones remaining at the points of attachment of the calyx to the circumference of the papilla of

the pyramidal substance (Henle). Outside the circular layer, again, a varying number of longitudinal bundles are found, all being freely connected with each other by oblique bundles, and having marked septa of a fibrous perimysium.

(3) The *urinary bladder* is, in all essential parts, identical with the ureters; but its muscle-layers are very broad, and arranged like a complex hurdle-work. The inner and outer layers take a prevailing longitudinal course; the middle layers run mostly in a circular direction. The longitudinal bundles are more marked in the main walls of the bladder, while the circular fibers prevail at the place of transition into the ureters and the urethra, producing the internal sphincter muscle. These fibers are also well developed in the mucosa between the two orifices of the ureters —the trigonum. The diameter of the walls of the bladder varies from two to fifteen mm., according to its conditions of contraction and extension. The arteries enter the posterior wall of the bladder, and are traceable through the muscle-coat into the mucous layer, where they break up into a rich capillary plexus. The nerves are most numerous in the lowest portion of the bladder—the so-called neck.

(4) The *urethra* is a prolongation of the bladder, and presents a structure similar to that of the bladder in the female; while the male urethra, being a canal common to the urinary and the genital tract, is of a more complicated character.

The *female urethra* is lined with stratified epithelium; its mucosa holds a few racemose mucous glands; its muscle-layers consist of an inner longitudinal and an outer circular—the smooth fibers of the latter blending, at the periphery of the urethra, with the striated muscle-fibers.

The *male urethra* has a stratified epithelium. It is maintained by some authors that, in the whole cavernous and in a large part of the membranous portion, there is but one layer of columnar epithelia. As to the different portions of the urethra, the nature of the covering epithelium requires more exact studies than have yet been made up to the present time, and it is quite possible that there are individual as well as local differences. The epithelial prolongations, in the form of racemose mucous glands (so-called Littre's glands), are quite numerous along the mucosa of the urethra, more particularly along the posterior wall. These often exhibit very long and winding ducts, and but few acini; the ducts sometimes open into larger, funnel-shaped pits at the inner surface of the mucosa. The muscle-layer is double along

the urethra, the circular layer being most marked in the membranous portion, and freely connecting with the striped muscles which surround this part. In the prostatic portion the longitudinal fibers are more developed—especially, it is maintained, in the region of the colliculus seminalis. The cavernous portion has a limited amount of longitudinal and circular bundles of muscle-fibers. The veins of the urethra, according to Henle and C. Langer, produce a plexus in the submucous layer, which is very large, especially in the prostatic and membranous portions, and is distinctly marked, also, in the cavernous portion from the cavernous body of the urethra proper. The latter is composed of comparatively narrow venous spaces, inclosed by trabeculæ of a fibrous connective tissue, which hold numerous small bundles of smooth muscle-fibers. At the periphery the cavernous body is insheathed by a layer of very dense, fibrous connective tissue—the tunica albuginea—which is also provided with bundles of smooth muscle-fibers, being mostly circular, and connected with those of the trabeculæ of the cavernous body.

XX.

THE URINE.

MANY hundred microscopic examinations of urine, made by the authority of the attending physicians of the patients, and further corroborated by post-mortem examinations, have enabled me to reach a certain degree of positiveness in the diagnosis of the diseases of the genito-urinary tract. As perfection in any department is reached only after a great deal of practice, the microscopic analysis of the urine also requires a thorough study, which, however, is greatly facilitated by the guidance of a reliable and experienced teacher.

I have published a part of the results of my examinations of the urine with the microscope, in previous years.* In my conviction, it is in vain to study the sediments of urine without a thorough knowledge of the minute anatomy of the kidneys, and in vain will any one endeavor to understand the kidneys without being thoroughly acquainted with their constituent tissues — connective tissue, blood-vessels, nerves, epithelia. The knowledge of the structure of the kidney involves the knowledge of the whole histology.

Normal Urine. Normal urine is a yellowish, transparent liquid, of a peculiar odor, slightly acid, neutral, or slightly alkaline. The reaction depends greatly upon the food or medicines taken,

* "The Aid which Medical Diagnosis receives from Recent Discoveries in Microscopy." *Archives of Medicine*, February, 1879. "Diagnosis of Vaginitis and Metritis, by Microscopic Examination of Urine." "Transact. of the New-York Patholog. Society." *The Medical Record*, July, 1880.

and it is one of the many physiological puzzles why the kidney epithelia produce, from the alkaline blood, acid urine. The specific gravity varies between 1.015 and 1.022, which depends entirely upon the amount of liquid taken into the body and the nature of the food. The average amount, in twenty-four hours, is 1550 c. c.— the solid ingredients representing sixty to seventy grammes (925 to 1080 grains).

The organic constituents of the normal urine, held in solution, are urea, uric acid, oxalic acid (bound to lime), hippuric acid, lactic acid, creatinine — the so-called extractive and coloring matters (xanthine, indican) — and, according to Brücke, grape-sugar. The inorganic constituents are chloride of sodium, phosphate of soda, magnesia, and calcaria; sulphates of alkalies and ammonia salts (in the coloring matters). The gaseous constituents are carbonic acid, nitrogen, and oxygen.

Normal urine is of watery consistence, foaming, if shaken, though the foam soon disappears when at rest. Sometimes the urine gives out a repulsive odor after standing for a short time; it has a pleasant violet scent after the inhalations of turpentine, and a highly unpleasant odor after the eating of asparagus.

If left at rest, normal urine exhibits a slight, cloudy sediment — more marked, as a general thing, in the urine of women. This consists of mucus, a few flat epithelia from the bladder or the vagina, and mucous corpuscles, which appear as finely granular (hydropic or swelled) plastids in a small number. This sediment commingles easily with the urine upon slightly shaking it. After sexual intercourse, both the male and female urine — the male, also, after a "wet dream"— contain large numbers of spermatozoids. Female urine, at the time of menstruation, contains a large amount of blood-corpuscles. As a matter of course, these constituents have no pathological significance.

After standing for one or more days, fungi appear in the urine. The rapidity of their development depends upon the height of the temperature of the surrounding medium. In acid urine, especially oïdium, the seed of mildew and afterward the mycelium of mildew, leptothrix, and bacteria, are found, which under these conditions grow very large, and, as a rule, are motionless or moving slowly. Oïdium varies in size from a small, homogeneous granule of high refracting power, to a globular or ovoid body, surpassing in diameter considerably that of red blood-corpuscles. So far as I have seen, we have no reason to discriminate between "yeast-plant" (Saccharomyces urinæ

cerevisiæ, lactis, etc.) and "oïdium," for they are identical in all essential features, as demonstrated by W. Hassloch (see page 40). Alkaline urine, or an originally acid urine which has become alkaline, under the above-named conditions develops micrococci, bacteria, and leptothrix, which are smaller and in more active motion the more alkalescent the urine becomes. Alkaline urine sometimes holds the so-called sarcina form, consisting of small granules grouped in rectangular lines; this is kindred to oïdium, and probably but one of the varieties in which mildew appears.

Pathological Urine. In pathological conditions the urine may be passed as a cloudy liquid of a consistence more or less deviating from that of water. The highest degrees of inspissation are reached in chronic cystitis, when the urine, being highly alkaline and decomposing in the bladder, appears as a viscid, stringy, muco-purulent mass, in which are found large quantities of pus-corpuscles and phosphates, has a repulsive ammoniacal smell, and exhibits varying numbers of clustered micrococci; a high degree of color is reached, without an increase of consistency, when biliary matters are present in the urine. Both color and consistency are considerably augmented when the urine is mixed with blood.

A highly acid reaction is due to the presence of a pathological amount of urea and urate of soda, in fever urine; also to a red extractive matter (uro-erythrine). In many instances, especially after abundant meat-eating and after intense bodily strain, and in slight disturbances, such as catarrhal inflammation of the mucosa of the respiratory tract, the mucosa of the stomach, and that of the intestine, in diarrhœa, the urine may be found laden with uric acid and urate of soda, which under such circumstances does not indicate a serious pathological condition. Women, in the disturbances preceding menstruation, often void highly acid urine. This, upon passing through the urethra, produces a slight, burning sensation in the mucosa.

Highly alkaline urine is voided by persons suffering from chronic cystitis, from chronic inflammation in any part of the body, especially in later stages of chronic encephalitis and myelitis. A transient, highly alkaline condition has no pathological significance; but if this condition is lasting, it points to some serious ailment in the organism. I have several times observed highly alkaline urine, laden with phosphates, as a symptom preceding nephritis.

The *amount of the urine* is greater the more liquid is taken into the body: Lager-beer, for instance, yields excellent diuretic results. Necessarily such watery urine has a very low specific gravity. It is maintained that by profuse drinking of water also the sum total of the excreted salts is increased, and "hydropathic doctors" attribute their success in curing all sorts of diseases to the "washing out" of the body, especially of the kidneys. Bodily exercise — for instance, gymnastics — increases the quantity of the excreted salts, without any increase of the watery constituents of the urine. A great quantity of a watery urine is voided in cold weather, when the perspiratory secretion is reduced or suspended; furthermore, certain alkaloids, such as those of laudanum, of coffee, tea, etc., stimulate the secretion of urine. Nervous excitement, anxiety, fear, hard mental work, sexual excitement, hysteric "fits," etc., produce the same effect. A very "nervous man" told me that he had to micturate quite frequently whenever he was about to write a "serious letter."

The amount of urine is, though not constantly, increased in diabetes; the color of diabetic urine is straw-yellow, its specific gravity reaches the highest point—*i. e.*, 1.040; and so does the amount of the solid constituents, grape-sugar sometimes reaching two hundred grammes in twenty-four hours.

The amount is considerably increased with a decrease of the solid constituents in cirrhosis of the kidneys. One of the most important clinical features of this disease is the constant voiding of large quantities of a watery, nearly colorless urine, almost completely destitute of salts.

The amount of urine is considerably reduced in intense bodily strain, accompanied by free perspiration, often notwithstanding profuse drinking, and in the beginning and acme of all acute inflammatory diseases of the organs.

Pathological constituents of the urine, variously combined with normal constituents, are, besides the before-mentioned grape-sugar and biliary matters, the following: albumen; the epithelia of the bladder in large quantities, and epithelia of the prostate, the pelves of the kidneys, and the kidneys; in the female, besides epithelia of the vagina in larger quantities, those from the cervical portion of the uterus and from the mucosa of the uterus. Furthermore, blood, if not due to menstruation; pus-corpuscles, leucine and tyrosine and cystine, oxalate and carbonate of lime in larger quantities; fat-granules and fat-globules, tubular casts, and shreds of connective tissue.

Albumen is not always a pathological feature, since there are persons who, after heavy meals, void small amounts of albumen without exhibiting any symptoms of kidney disease. It

invariably accompanies the severe forms of nephritis, and larger quantities of pus and blood in the urine. Albumen, on the contrary, may be absent in grave cases of catarrhal nephritis and cirrhosis of the kidneys. In very rare cases of so-called chyluria, cloudy urine is secreted of a high specific gravity, so rich in albumen that it coagulates into a thick jelly upon being boiled. In addition to the albumen, which is always held in solution, unless acids be added or the urine boiled, numerous fat-granules are present in chyluria, which render the freshly passed urine opalescent. Lastly, a small number of plastids, of the aspect of lymph-corpuscles, may be found. The disease in most cases terminates fatally, and the kidneys, it is maintained by good pathologists, are found normal.

Determination of the Specific Gravity. According to Hofmann and Ultzmann, we ascertain the exact specific gravity by means of the urinometer, as follows: Fill a standing glass cylinder four-fifths full of urine. The froth being removed by filtering-paper, the urinometer is placed in the urine, never being allowed to come in contact with the walls of the vessel. Bring the eye on a level with the surface of the urine, and read the corresponding division of the urinometer, but not the upper rim of the fluid raised a little by attraction. Touch the stem, causing the urinometer to sink slightly in the fluid, and, after it has come to rest, read again. In all such observations the urine should have a temperature of at least 62° F. (17° C.); otherwise considerable error may result. If the amount of urine is small, dilute with even three or four volumes of water; test as directed, and multiply the number of the division mark by the number of volumes used for dilution. For example, if three volumes of water be added to one volume of urine, and we read 1.008, to obtain the real specific gravity of the original fluid 1.008 is multiplied by $1+3=4$ ($1.008\times4=1.032$). The solid materials, on which the specific gravity depends, which were dissolved in one volume, are, after the dilution, dissolved in four volumes; the specific gravity is therefore only one-fourth of that of the original. By multiplying the decimal of the specific gravity by the coefficient of Häser (2.33) we have the result in grammes of the weight of solids contained in 1000 c. c. of urine. Hence, if we have the entire amount passed in twenty-four hours, we can easily estimate the weight of solids of the whole. For example, we have 1500 c. c. passed in twenty-four hours, of specific gravity 1.020; to estimate the weight of solids in 1000 c. c. we multiply the decimal 20 — the last two figures — by the coefficient 2.33 ($20\times2.33=46.60$), and the product, 46.60, is the weight in grammes of the solids in 1000 c. c. of the urine. Valuable conclusions may be drawn from the amount of solids and the specific gravity; but each case requires special consideration. For example, we may have to deal with diseased kidneys, the amount of urine being normal or diminished, of a low specific gravity. We may conclude, since urea composes nearly the half of the solid constituents, that urea has not been excreted in a sufficient quantity, and we may consequently expect uræmia very soon.

Chemical Tests. For practical purposes the chemical examination of the urine is very simple. Quantitative analysis is of comparatively small value, as all ingredients of the urine, at least after it has stood for a day or two, become visible with the microscope, and the amount of *urea*, which, as such, cannot be seen under the microscope, is in a constant proportion to the uric acid and its salts. It forms at least the half of all the organic constituents.

The urine, as brought for examination, is either transparent or cloudy. After the sediment has been deposited, we pour a small portion from the upper parts of the liquid into a test-tube, immaterial what reaction the urine may give, and boil it over a spirit-lamp. The results are as follows:

(a) The urine is transparent, and by being boiled remains unchanged; if a small sediment is present in the original fluid, this feature indicates normal urine.

(b) The urine is transparent, but after boiling becomes cloudy. By adding a few drops of acetic acid, the urine clears up, and this shows an increased amount of phosphates; if effervescence occurs upon the addition of the acid, carbonate of lime or carbonate of ammonia is present. If the cloudiness remains after the addition of the acid, we know that albumen is present, and, if in large quantities, the urine is converted into a consistent, jelly-like mass, easily spattering during the process of boiling. From the sediment of the acidulated urine collected at the bottom of the test-tube, an approximative estimation of the amount of albumen may be made.

(c) The urine is cloudy, and by being boiled clears up entirely. This means an excess of the urates, especially of the urate of soda.

(d) The urine is cloudy and remains so after boiling, or increases in cloudiness. The same process must be resorted to as in case *(c)*, with the same diagnosis.

(e) The urine is cloudy and remains unchanged by boiling and by addition of acetic acid. This proves the presence of a large amount of the organisms of decomposition, micrococci, bacteria, and leptothrix in alkaline urine, and oïdium or fully developed mildew in acid urine.

An important chemical test is that for grape-sugar. Suspicion arises of its presence, when for some time a large quantity of a straw-yellow colored urine of a high specific gravity is passed. Small quantities of grape-sugar may be present temporarily and

without any of the named features. This form of diabetes has no clinical significance. Not any of the tests for sugar taken alone are entirely reliable, and for a thorough determination of its presence several methods must be resorted to.

Tests for Sugar. (*a*) *Moore's Test.* Pour into a test-tube two volumes of urine and one volume of hydrate of potassa, and heat to boiling. Phosphates, if precipitated in a larger quantity, must be filtered off. When the fluid becomes hot, according to the amount of sugar present, a lemon-yellow, a yellowish-brown, or a blackish-brown color appears. By addition of a few drops of nitric acid the liquid loses its dark color and gives out an odor like molasses. The addition of KOH to cold urine may produce a dark color, which is due to the presence of coloring matters of the bile.

(*b*) *Böttger's Test.* Pour into a test-tube two volumes of urine and one volume of KOH; add subnitrate of bismuth in a quantity held by the point of a pen-knife and heat for a short time. If sugar is present, it reduces the bismuth salts to the black suboxide of bismuth. Small quantities of sugar will render the bismuth salts slightly gray. Albumen must be eliminated by boiling and filtration, if present in larger quantities.

(*c*) *Trommer's Test.* Pour two volumes of urine into a test-tube, and add one volume of KOH or NaOH (solution 1 : 3); add, drop by drop, a solution of sulphate of copper (solution 1 : 10), and shake until the mixture shows a blue color. Heat the mixture, without boiling: if sugar is present, the copper-salt is reduced in such a way that at first yellow cuprous hydroxide, and afterward a red sediment of cuprous oxide is formed. Albumen, if present in large quantities, must be removed first by coagulation and afterward by filtration. The yellow color of the mixture alone indicates either a small quantity of sugar or an excess of urates. Mucus in large quantities also reduces the sulphate of copper in the same manner as sugar. If no sugar is present, the mixture assumes a dirty grayish-green, and no red precipitate appears at the bottom.

(*d*) An approximate estimation of the amount of sugar present, which is not admissible by simply considering the specific gravity, may be made by the method of Vogel of boiling two volumes of urine with one volume of KOH. A one per cent. solution of sugar assumes a canary-yellow; a two per cent. solution a dark amber; a five per cent. solution a brown-red color, the liquid remaining transparent; while a ten per cent. solution is rendered dark brown and opaque.

(*e*) *Roberts' Fermentation Test.* Into each of two bottles—one of four ounces, the other of twelve ounces capacity—four ounces of the urine are poured. A piece of fresh yeast, the size of a walnut, is added to the urine in the larger bottle, which is closed with a cork nicked for the escape of gas evolved by fermentation. The smaller bottle is tightly corked, and the two bottles are placed side by side in a uniform temperature of 68° to 75° F. At the end of twenty-four hours the subsidence and clearing off of the scum from the urine in the larger bottle will announce the completion of the fermentation. The specific gravity of each specimen is carefully taken by an accurate urinometer, when any difference of specific gravity will indicate sugar, and the number of degrees of difference the number of grains per fluid ounce. For example, if the specific gravity of the unfermented urine is

1032, and that of the fermented urine 1020, the urine contains twelve grains of sugar to the fluid ounce. This test, although not accurate to the smallest fraction of a grain, is clinically all that is needed for ordinary quantitative work.

(*f*) *Fehling's method* is the most reliable for volumetric determination of the amount of sugar. Fehling's solution contains in a volume of 1000 c. c. the following: 30.639 grammes of cupric sulphate, 173 grammes of pure crystalline tartrate of sodium and potassium, and 500 grammes of a solution of caustic soda of specific gravity 1.12. Of this solution 10 c. c. are reduced by 0.05 gramme of sugar.

Microscopic Examination. The urine, in an amount of four to six ounces, is left at rest for at least six hours—still better for twelve hours—either in an ordinary bottle of white glass, or in a funnel-shaped champagne-glass. The sediment formed at the bottom of the vessel is the subject for microscopic analysis, after the transparent portion has been carefully decanted. We transfer a droplet to the slide by means of a camel-hair brush or a pipette; the former answers all purposes if it is cleansed thoroughly with water after each examination. To preserve urine, we use either simple glycerine mixed with the sediment, and left at rest in a broad, open vessel until the surplus water has evaporated; or a small amount of alcohol can be added before the admixture of glycerine. Pus-corpuscles, epithelia, and casts are best preserved by adding to the whole amount of urine a few drops of chromic acid solution, enough to precipitate the albumen and the other constituents. After several weeks the liquid may be decanted and a few drops of alcohol added to the sediment, to prevent the growth of mildew.

Before entering the study of urine, the extraneous matters must be well known. In Fig. 357 the most common are illustrated.

Silk-fibers are homogeneous, moderately shining; their cut ends are flattened by the blades of the scissors, and rendered slightly jagged. If woven, the single fibers assume wavy or spiral impressions from their neighbors, and under these conditions are also flattened.

Linen-fibers are composed of smaller fibrillæ and show transverse fractures or breaches, caused by the process of hatcheling. The finest fibrillæ are broken off irregularly from the surface of the main fiber.

Cotton-fibers are flat, wavy, and twisted, and are more compact along the edges than in the center; the central portion may show irregular breaches, or it may be absent if the compact edges are pressed together.

Wool-fibers have serrated edges, corresponding to the edge the covering imbricated scales of the cuticle; the structure is ıtly striated. Hairs of different animals have different forms; central medullary canal, as well as a varying amount of pig-

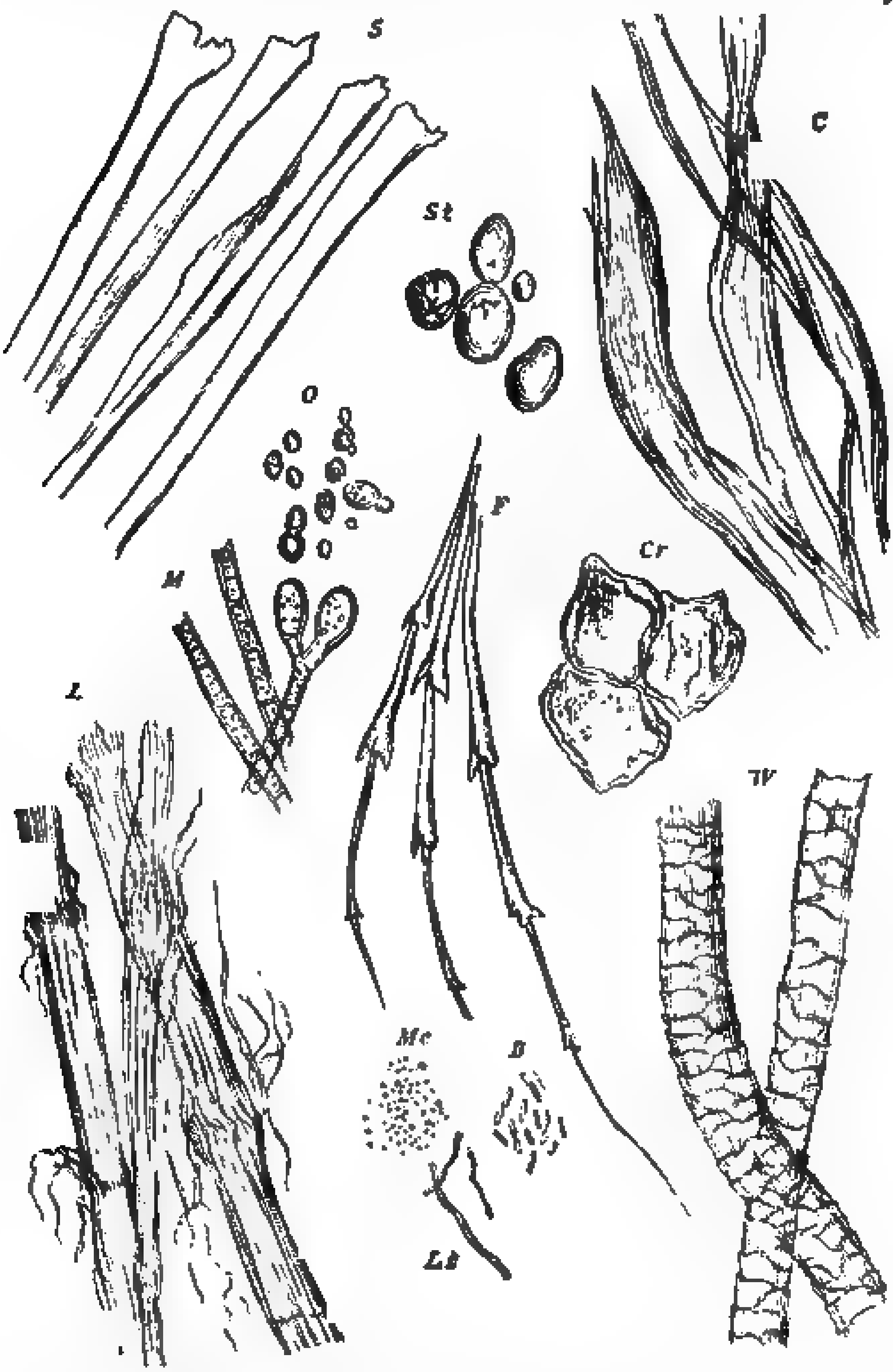

FIG. 357.—ACCIDENTAL OCCURRENCES IN THE SEDIMENT OF URINE.

t, silk fibers, *C*, cotton fibers, *L*, linen fibers, *W*, sheep's wool, *F*, feather; *St*, starch-ıules of rice; *Cr*, cork particles, *O*, oidium, the seed of mildew, *M*, mycelium of mildew; micrococci; *B*, bacteria, *Lt*, leptothrix. Magnified 500 diameters.

ınt, may be observed. If the cuticle is removed from sheep's ıol, it is termed shoddy.

Any of the above-named fibers may be found dyed in different colors.

Feather appears in single barbules, or in the shape of branching formations; the ends of the barbules are whip-like, the size of the links gradually decreasing toward the terminations. *Scales from the wings of insects* are also found; these are delicate, serrated plates, with a stem-like projection.

Of *vegetable matters* the most common are oïdium and mycelium of mildew, bits of cork, charcoal particles, pollen of plants, mostly the seed of lycopodium (globular formations with a distinct shell, studded with thorny projections), and particles of wood. Starch-granules are very common in female urine, being used for powdering the genitals. In acid urine, motionless leptothrix and bacteria are found; in alkaline urine, micrococci, bacteria, and leptothrix in active motion.

It must be known that flaws, which often present the shape of butterflies' wings, scratches of the covering-glass, rust-particles in both the cover and the slide, often occur. A physician brought me a specimen of a worm-shaped mass of rust in the cover, which he mistook for an unknown parasite. He claimed having seen the parasite quite often, and I discovered that he had used the same cover for examination of the urine of a patient.

Crystalline Sediments. The crystalline formations found in urine belong either to the group of acids and acid-salts, or to the groups of alkaline salts. The *acid sediments* are uric acid, oxalate of lime, urate of soda (amorphous), and hippuric acid. The first three are very common sediments, while hippuric acid is rare. Still rarer are cystine and tyrosine, which also belong to this group. The *alkaline sediments* are urate of ammonia, triple phosphates, calcium phosphates (which appear both as amorphous and crystalline sediment), and calcium carbonate (amorphous and crystalline). Magnesium phosphate is exceptional.

(1) *Uric acid* is a constant ingredient of the urine of carnivora. Its amount is greatly augmented by rich animal and vegetable food, by acute febrile diseases, by impeded function of the heart, the lungs, the kidneys, the diaphragm, etc. It is decreased in profuse secretion of urine, and in the later stages of nephritis, when the secretion of all salts is interfered with. It is also increased by bodily exercise. Its amount varies greatly at different times in the urine of the same person.

Uric acid appears in lozenge-shape (rhomboidal prisms), with numerous variations, and has always a brown or red-brown color,

except when precipitated in very thin plates. It is often collected in star-shaped groups of varying sizes, and produces the so-called brick-dust sediment. In super-acid urine, which is

FIG. 358.—URIC ACID.

U, common crystals; U^1, crystals from over-acid urine; U^2, clusters (gravel) of uric acid from the pelvis of the kidney. Magnified 300 diameters.

often combined with gouty and arthritic processes, or with the formation of uric acid concretions in the bladder, it appears in peculiar spear-, comb-, and brush-shapes. The concretions originating in the pelves of the kidneys (so-called uric acid gravel) are comparatively large masses, composed of minute crystals of uric acid. (See Fig. 358.)

(2) *Oxalate of lime* is frequently mixed with uric acid, and, if present in small quantities, has no pronounced significance. Oxalic acid, being a product of uric acid, has a special affinity for calcium, and appears in the sediment—often very late and only in the shape of oxalate of lime. In derangements of digestion (dyspepsia) and disturbances of the nervous system ("nervousness," "neurasthenia," etc.) its amount is greatly augmented. It appears in the form of quadrilateral octahedrons, with the characteristic letter-envelope-like line in front view, while in edge view the octahedral form is most marked. The refracting power of these crystals is very high, and they are without color. Their size varies from the smallest dot-like squares up to crystals of quite considerable size, which, however,

FIG. 359.—OXALATE OF LIME.

O, ordinary crystals of varying sizes; O^1, rare forms. Magnified 300 diameters.

are usually smaller than those of uric acid. Sometimes twin formations of octahedrons are observed. Very rarely it appears in the shape of concentrically striated disks or of dumb-bells. (See Fig. 359.)

(3) *Urate of soda* appears in larger quantities under the same conditions as uric acid, with which it is combined, especially in febrile conditions. This salt produces the very common so-called clay-water sediment. It presents fine, amorphous granules of a dark brown color (very rarely colorless, and resembling coagulated albumen), in a moss-like arrangement. It adheres easily to foreign bodies (fibers) present in the vessel, and also to mucus and epithelia. When the urine after standing becomes alkaline,

FIG. 360.—URATE OF SODA.

S, ordinary form; *S*¹, rare form; *S*², forms of transition of urate of soda into urate of ammonia. Magnified 300 diameters.

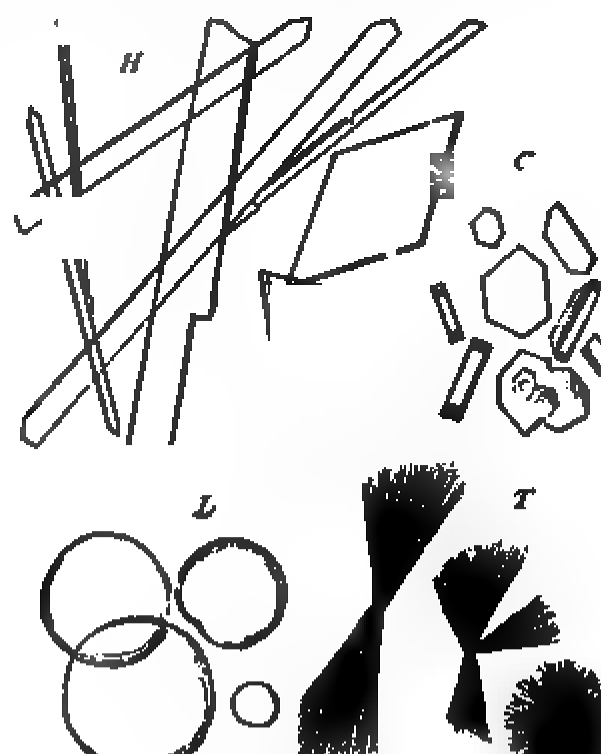

FIG. 361.—RARE SEDIMENTS OF ACID URINE.

H, hippuric acid; *C*, cystine, *L*, leucine, *T*, tyrosine. Magnified 300 diameters.

the granules appear in the shape of delicate dumb-bells and increase in size, both features being characteristic of urate of ammonia. Uric acid crystals, under the same conditions, break up into clusters of brown globules, which for a while still retain the original lozenge-shape. A rare form of urate of soda is that of needles arranged like sheaves of wheat (Ultzmann). (See Fig. 360.)

(4) *Hippuric acid* is of common occurrence in herbivorous animals, especially in the urine of horses; while in the urine of

man it is very rare, and mostly observed after administration of benzoic acid preparations, and sometimes also in diabetes. (See Fig. 361).

Cystine is a rare sediment, which sometimes produces concretions in the bladder; it consists of hexagonal, colorless plates, which in side view show (one) perfect facet, and (two) imperfect neighboring edge-facets. It is readily soluble in ammonia, which is one of the features distinguishing it from uric acid. In certain families it is said to be of regular occurrence in the urine. (See Fig. 361.)

Tyrosine appears in the form of needle-shaped crystals, grouped in clusters or sheaves, crossing at various angles. It is usually accompanied with *leucine*, which resembles flat, colored drops of fat of a large size, with delicate radiating and concentric striations, but is insoluble in ether. These rare sediments are observed in cirrhosis and yellow atrophy of the liver, and in cases of phosphorus-poisoning. (See Fig. 361.)

(5) *Urate of ammonia* is found in fresh urine only when passed in a decomposed and markedly alkaline condition, such as occurs in chronic catarrhal cystitis. In alkaline urine this is a very common sediment in connection with triple and simple phosphates. It appears as brown globules of varying sizes, exhibiting faint concentric and radiating striations. The globules may appear single or in clusters of several coalesced spheres, either smooth or provided with thorny, sometimes branching and curved offshoots—the so-called thorn-apple shape. (See Fig. 362.)

FIG. 362.—URATE OF AMMONIA.

Dark brown globules. Magnified 300 diameters.

(6) *Triple phosphates* (combined ammonium and magnesium phosphates) appear as colorless, highly refracting, rhomboidal crystals, varying greatly in size. If incompletely developed, they represent thin plates or cross-like formations without facets. In normal urine they are found only in small quantity, but are considerably increased in chronic inflammatory processes, also in so-called rheumatic and arthritic diseases, and in osteitis. They easily dissolve by the addition of an acid. (See Fig. 363.)

(7) *Simple phosphates* (calcium and magnesium phosphates) appear in alkaline urine in the form of *amorphous*, highly refracting granules, without color, and usually clustered together, occasionally in a moss-like arrangement, or in the shape of *rosettes*, composed of pointed spiculæ, the points of which are united at the center of the rosette, while each spicula may have a uniform

diameter or be broadened toward the periphery of the rosette. All these formations are highly refracting and colorless. Their significance is the same as that of triple phosphates. (See Fig. 364.)

(8) *Calcium carbonate* is the most common sediment in the urine of herbivorous animals, and the turbidity of their urine is due to its presence. In man this salt is of infrequent occurrence—appearing, together with the phosphates, in the shape of fine granules or dumb-bells. It is observed, in combination with magnesium salts, as delicate prisms. It appears mainly in inflammatory and carious processes of the bony system. The addition of acid produces an effervescence of this salt, as well as of ammonium carbonate. (See Fig. 364.)

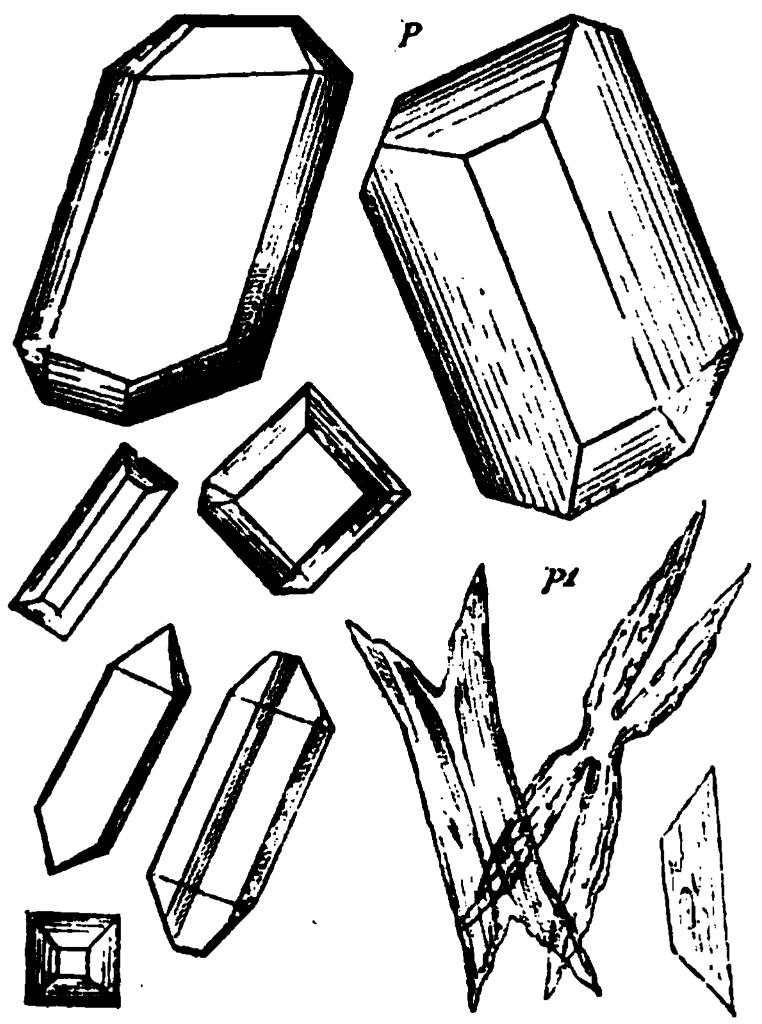

FIG. 363.—TRIPLE PHOSPHATES.

P, perfectly developed crystals; *P*1, imperfectly developed crystals. Magnified 300 diameters.

Magnesium phosphate is observed in urine after the internal use of the fixed alkali-carbonates, such as are held in solution by many mineral waters. It produces elongated quadrilateral plates.

Mucus occurs in varying quantities in normal urine, more especially in the female. It appears as finely striated, scarcely perceptible strings, being a physiological product of the epithelia. Slight irritation of the mucosa by acid urine laden with uric acid and urate of soda, increases the amount of mucus, and, the urates being precipitated on it, the stringy masses become more easily perceptible. They may be mistaken for casts, as they bear some resemblance to them. Mucus-corpuscles, together with mucus-strings, are also observed, having the character of finely granular, sometimes nucleated, plastids. If sperm is admixed with the urine, its mucous constituent appears as pale, caky masses, entangled with spermatozoids. In chronic catarrhal inflammation of the mucosa of the urethra, the mucus-strings, voided from the ducts of the mucous glands, are very large, cylindrical, and twisted; they often are perceptible to the naked eye. The mucus secreted by the pros-

tate gland during sexual excitement contains numerous mucus-corpuscles, which, when originating from the columnar epithelia of ducts, are in part elongated. Mucus appears also as delicate, striated, and fringy cylinders, the so-called "mucous casts;" it is doubtful, however, whether they are ever produced in the uriniferous tubules.

Sometimes pale concentric formations are found in the male urine, which are so-called *colloid or amyloid corpuscles of the prostate gland* (prostatic concretions). Their number seems to be augmented mainly in hypertrophy of this gland.

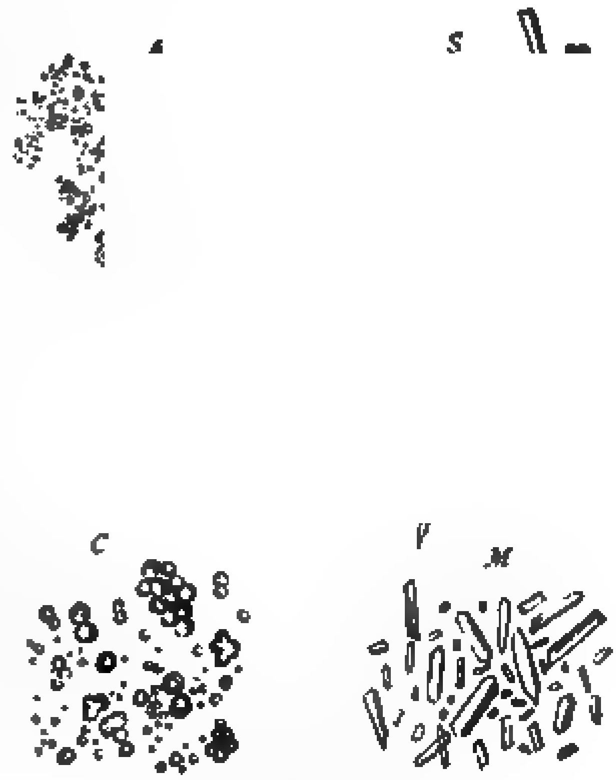

FIG. 364.—SIMPLE PHOSPHATES AND CARBONATE OF LIME.

A, amorphous simple phosphates, *S*, star-shaped simple phosphates; *C*, amorphous carbonate of lime, *M*, combination of carbonate of lime with magnesium salts. Magnified 800 diameters.

Pus-corpuscles always indicate an inflammation along the genito-urinary tract. Their origin was dwelt upon in the chapter on "inflammation"; here I wish merely to repeat that a large number of pus-corpuscles arise directly from the epithelia, by endogenous new formation of living matter. The pus-corpuscles are the best material for determining the general constitution of the patient, his chances for recovery, or the probable duration of his life (see page 62, Fig. 20). The presence of pus-corpuscles of the series *P* exclusively indicates a broken-down constitution, and the rapidly approaching death of the patient. Pus-corpuscles in freshly passed urine exhibit active amœboid form-changes, which may be observed exceptionally, even twenty-four hours after the urine has been passed. Pus-corpuscles, with delicate, hair-like prolongations (cilia), arise from the ciliated, columnar epithelia of the uterus; in freshly passed urine the cilia may show waving motions. Care must be taken not to mistake the cilia for bacteria adhering to the surface of the pus-corpuscles, and also exhibiting oscillatory movements.

In very dilute or highly alkaline urine, pus-corpuscles swell and assume a large, globular shape, the central portion being

occupied by the nucleus, while the peripheral portions show only a small number of granules. In highly ammoniacal urine, voided in chronic catarrhal cystitis, the pus-corpuscles, when present in a large quantity, by bursting and coalescence produce a sticky, slimy mass, which can be transferred to the slide only in coherent, jelly-like lumps. Upon evaporation of the specimen of urine kept on the slide, the pus-corpuscles present variously jagged forms, which should not be mistaken for the result of amœboid motion.

In chronic catarrhal cystitis, pus-corpuscles from pigmented epithelia of the bladder, to the presence of which is due the slate color of the mucosa, also exhibit a varying amount of dark brown pigment-granules. Pigmented pus-corpuscles at once justify the diagnosis of chronic catarrhal cystitis.

Pus-corpuscles which have arisen from epithelia of the pelves of the kidneys, or from those of the uriniferous tubules, sometimes contain delicate red-brown crystals of hæmatoidin. This indicates the presence of hæmatoidin in the epithelia, caused by a previous hæmorrhage. In recent hæmorrhage the pus-corpuscles may have a uniform yellow color, due to imbibition of the coloring matter of the blood.

Red blood-corpuscles are discoid bodies of a yellowish luster, in the fresh condition, and often crenated. After standing for a few days, acid urine may have the same influence upon the blood-corpuscles as dilute solutions of bichromate of potash (see page 64), inasmuch as many blood-corpuscles appear granular with low, and distinctly reticular with high powers. By the addition of a solution of chromic acid the same result may be obtained, though, as a rule, much less marked, and most of the red blood-corpuscles after treatment with chromic acid appear as pale, apparently structureless, double-contoured circles.

Extravasated blood, if retained within the tissues, changes to *hæmatoidin*, which appears both in the shape of minute, oblong rhombs, and needle-shaped, sometimes stellate, crystals of a brilliant red-brown color. Such crystals may be observed, as before mentioned, in the interior of pus-corpuscles. In a case of chronic abscess of the kidney I have seen large quantities of hæmatoidin admixed with the pus; the chronic condition could be diagnosed mainly from the presence of hæmatoidin.

Shreds of connective tissue are of frequent occurrence in the sediment of urine. They are seen either as delicate bundles or as bulky shreds, containing, in the latter instance, a varying

number of plastids (connective-tissue corpuscles). Their presence may be due to hæmorrhage, and, in this instance, they as a rule have a yellow tint from the coloring matter of the blood. Small shreds of bundles of connective tissue of a yellow color, if present with large quantities of blood-corpuscles and kidney epithelia, but without pus-corpuscles, indicate capillary hæmorrhages in the kidney. Large shreds are present whenever an abscess has emptied into the urinary tract, or ulceration has taken place either in the urethra (in strictures), in the bladder, or in the pelves of the kidneys. The accompanying epithelia enable us to determine the seat of the ulceration. Ulcers of the vagina, the cervical portion of the uterus, and its mucosa, may be diagnosed by the same means. When a papilloma is developed in the mucosa of the bladder, large shreds of connective tissue, containing blood-vessels in formation or fully developed, are exceptionally voided with the urine. Occasionally these shreds assume the shape of coils. (See Fig. 365.)

Shreds of connective tissue have a higher refracting power than mucous strings, but less than linen-fibers, and they cannot be mistaken for any of these formations. I have observed a large number of regular linen-fibers voided with the urine in a case in which external urethrotomy had some time previously been performed, and the surgeon had accidentally left a plug of lint in the urethra, which probably had found its way into the bladder.

Fat-granules and *fat-globules* are of very common occurrence in urine. The latter may be passed of quite a considerable size, and that such globules are really formed in the kidneys can be proved by direct observation (see page 777, Fig. 354). In many instances, however, fat is extraneous, due to impurity of the vessel or to the fat (oil, vaseline) used for lubrication of catheters and sounds, or the finger used for exploration of the female genitals. Small fat-granules are invariably found accompanied by albumen, and, after precipitation of the latter by an acid, the bright, glistening granules of fat, clustered together and varying in size, are easily distinguished from the albumen, the granules of which are pale and of a uniform size. The presence of fat-granules indicates fatty degeneration of the kidneys, and more certainly if fatty casts are also found. In this condition often a few red blood-corpuscles and shreds of connective tissue are mixed with the sediment, caused, perhaps, by a certain brittleness of the walls of the capillaries. In chylous urine fat-granules are formed in connection with albumen, without any kidney epithelia or pus-corpuscles. (See Fig. 365.)

Epithelia. An acquaintance with the epithelia found in urine is of the greatest importance, since it is only by an accurate knowledge of the point from whence they come that we are able to obtain a diagnosis of the location of the morbid process. Most of the morbid processes occurring along the genito-urinary tract are inflammatory in nature, and marked by the presence

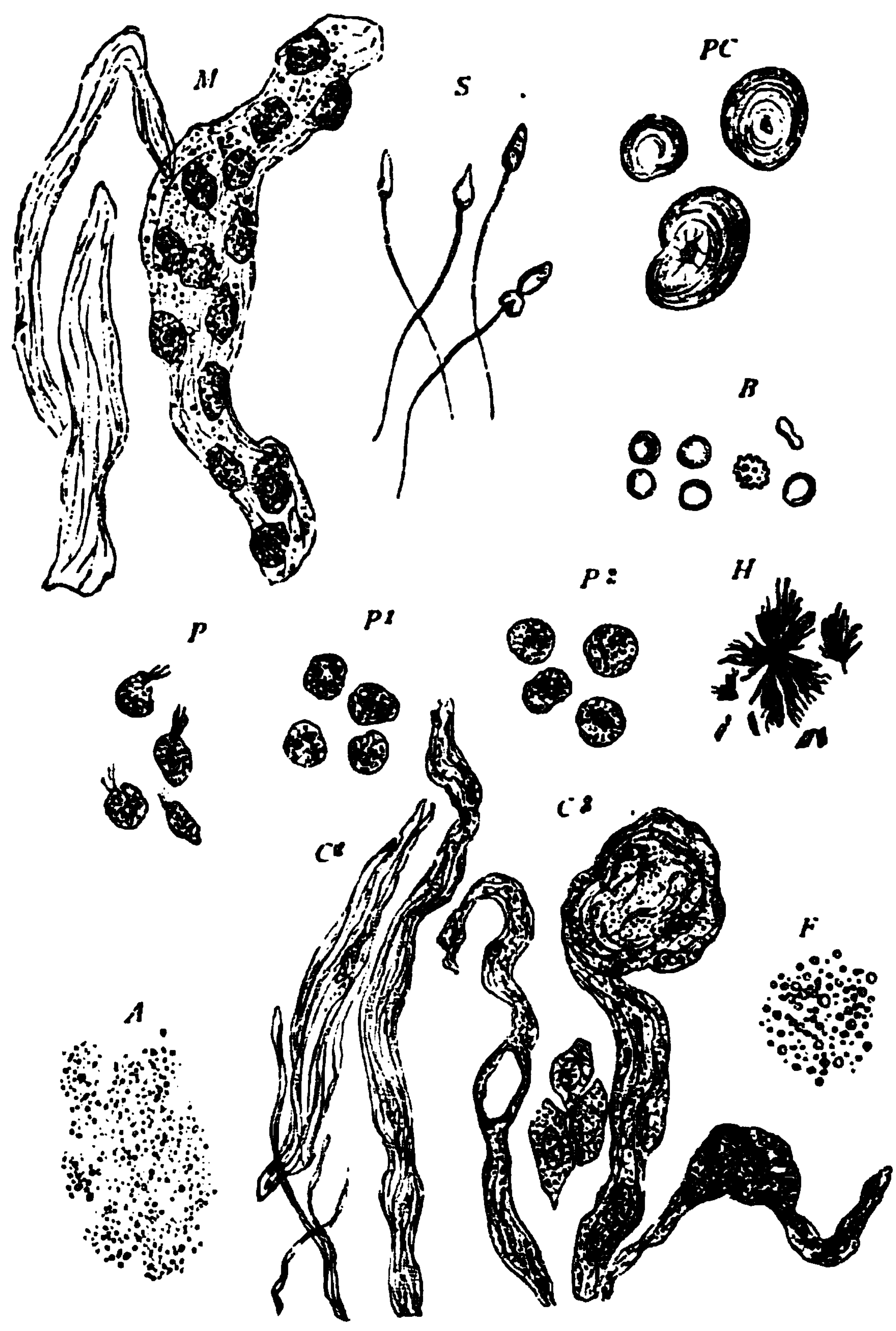

FIG. 365.—VARIOUS OCCURRENCES IN THE SEDIMENT OF URINE.

M, mucus-threads; *S*, spermatozoids; *PC*, prostatic concretions; *P*, ciliated pus-corpuscles; *P*1, pus-corpuscles, with pigment-granules; *P*2, pus-corpuscles, with hæmatoidin-crystals; *B*, red blood-corpuscles; *H*, hæmatoidin-crystals; *A*, coagulated albumen; *F*, fat-granules; *C*1, shreds of connective tissue; *C*2, débris of papilloma of the bladder. Magnified 500 diameters.

of pus-corpuscles in the urine; where the inflammation is located can be determined only by the epithelia. When pus-corpuscles are found unaccompanied by epithelia, which sometimes

occurs, we are unable to decide where the morbid condition is situated.

As a general thing, we know that in the male genito-urinary tract the urethra, the bladder, the ureters, and the pelves of the kidneys have a lining of stratified epithelia; while all glands in connection with the tract, the mucous glands, the prostate, and their ducts, including the ejaculatory ducts, have a single layer of epithelia. A single layer is present also throughout all the uriniferous tubules. The largest epithelia are found in the urethra; next in size are those of the bladder, then follow the epithelia of the pelves of the kidneys, and the smallest epithelia come from the kidneys proper. It is maintained that the epithelia of the bladder, of the ureters, and of the pelves of the kidneys, are identical in size and shape. By scraping off the epithelia of the above-named organs, this idea appears correct; but, if we study the epithelia *in situ*, we arrive at the conviction that the epithelia, upon approaching the kidneys, very gradually decrease in size from without inward. Middle-sized epithelia of the bladder are identical with the largest pelvic epithelia, and, therefore, are of no value for diagnosis, while the average epithelia of the pelves are distinctly smaller than those of the bladder. The caudate, double caudate, and lenticular forms of epithelia are far more prevalent in the pelves and calices than in the bladder, and well adapted, therefore, for a diagnosis of pyelitis.

In the female genito-urinary tract, the epithelia of the vagina, the cervical portion of the uterus, the urethra, bladder, ureters, and pelves, are stratified. The epithelia of the mucosa of the uterus are columnar and ciliated, forming a single layer; the kidneys also show columnar, flat, and cuboidal epithelia in a single layer, the same as in the male. Flat and cuboidal epithelia of the kidney, in the urine of either sex, cannot be distinguished, but the columnar epithelia are distinctly marked formations. Besides, in either sex, flat, horny epithelia from the fingers and the external genitals may be found, having a jagged contour, a high refraction, a homogeneous appearance, and no nucleus. They often are studded with particles of dust or granules of fat. Epidermal scales from the inner surface of the prepuce and that of the labia majora are paler, and often hold granules of fat (sebaceous material).

The diagnostic value of the epithelia in urine, if mingled with pus-corpuscles, is as follows (see Fig. 366):

Male Urine. The largest flat epithelia from the urethra are

occasionally seen, *i. e.*, in the initial stage of catarrhal or blennorrhoic inflammation; the largest columnar epithelia from the urethra occur in deeply seated blennorrhoic inflammation and in ulceration, which often lead to the formation of a stricture.

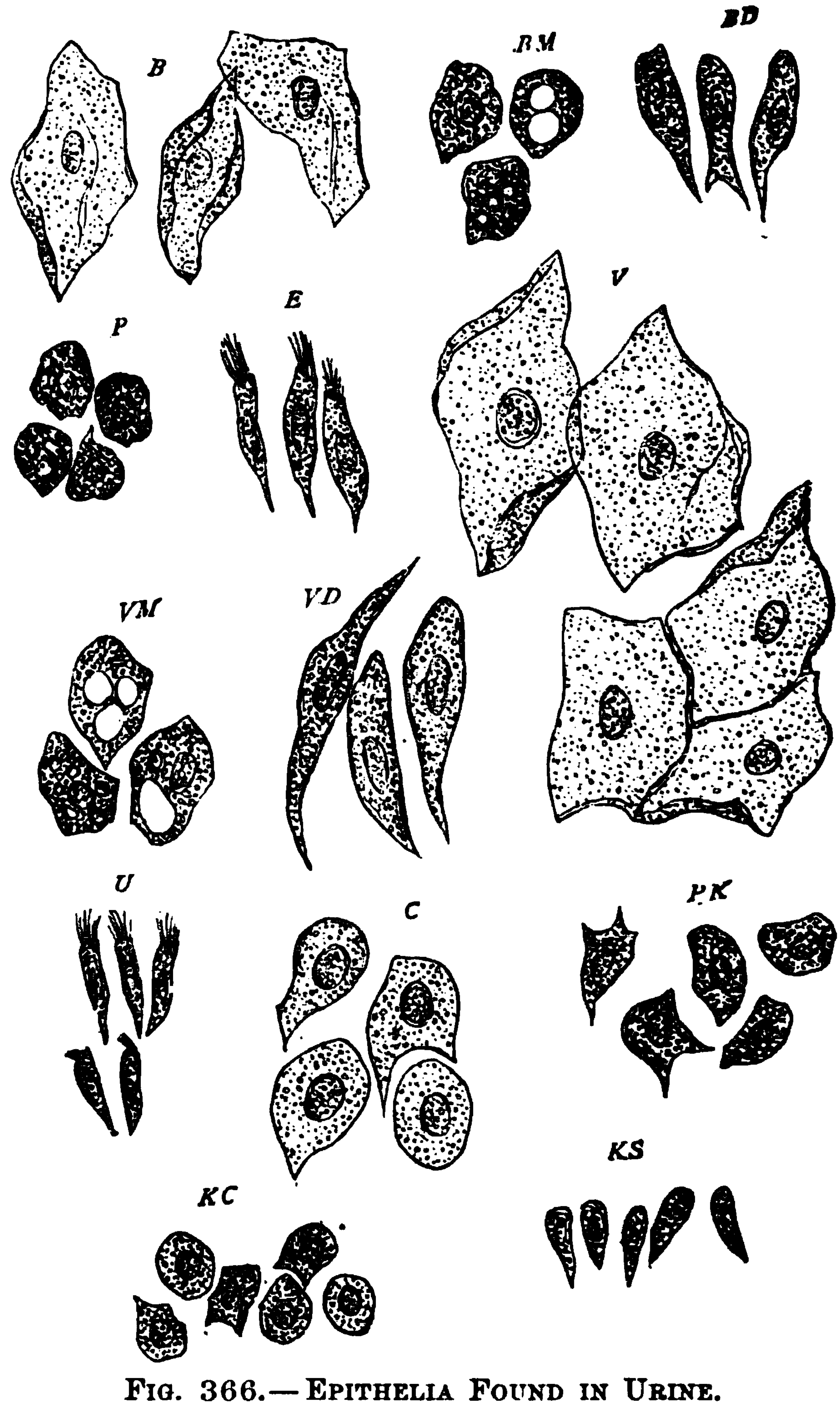

FIG. 366.—EPITHELIA FOUND IN URINE.

B, bladder-epithelia from upper layers; *BM*, bladder epithelia from middle layers; *BD*, bladder epithelia from the deepest layer; *P*, prostatic epithelia; *E*, epithelia from the ejaculatory ducts; *V*, vaginal epithelia from upper layers; *VM*, vaginal epithelia from middle layers; *VD*, vaginal epithelia from the deepest layer; *C*, epithelia of the cervix uteri; *U*, epithelia of the mucosa of the uterus; *PK*, epithelia from pelvis of the kidney; *KC*, kidney epithelia from the convoluted tubules; *KS*, kidney epithelia from the straight collecting tubules. Magnified 500 diameters.

Cuboidal epithelia, somewhat smaller than the average cuboidal epithelia of the bladder, come from the prostate in catarrhal prostatitis and hypertrophy of the prostate. Ciliated columnar epithelia, distinctly surpassing in size those from the mucosa of the uterus, indicate slight catarrhal inflammation of the ejaculatory ducts. They are rarely seen ciliated, as the cilia break off very easily; but delicate parallel rods in the interior of the epithelia, near their basal surface, indicate that the epithelia were originally ciliated.

Female Urine. The large, flat epithelia from the vagina are very common occurrences, and indicate catarrhal vaginitis; they appear singly or in clusters, and are often studded with micrococci. The largest cuboidal and columnar epithelia from the vagina are observed in cases of intense, deeply seated, or ulcerative vaginitis.

Flat and cuboidal epithelia, smaller in size than those of the vagina, and, as a rule, finely granular, often with offshoots, are shed from the cervical portion of the uterus. If present with pus- and blood-corpuscles and shreds of connective tissue, they indicate ulceration of the cervix.

It must be borne in mind that cuboidal epithelia are originally angular, polyhedral formations, but, by swelling in the urine, assume a more or less regular—nay, perfectly spherical, form. The size of the spheres, however, is sufficient for a diagnosis of their previous location. If destined for microscopic examination, care must be taken not to have male and female urine mixed, which might easily happen in married life. On account of such a mixture I once mistook the sex. In this case, besides vaginal epithelia, starch-granules were also present in large numbers. The gentleman denied the use of powder, and his clean urine afterward settled the question.

I have seen *prostatic epithelia* of the male, and *cervical epithelia* of the female, of a higher refracting power, a nearly homogeneous, waxy look, with an indistinctly marked nucleus, in persons affected with syphilis. In a number of cases, from these appearances I have correctly diagnosed syphilis; but my experience in this respect is too limited yet for announcing that the waxy metamorphosis of the above-named epithelia is always due to syphilis. There may be other chronic ailments of the system, or of the organs from which the epithelia were cast off, producing the same appearance.

Delicate columnar, ciliated epithelia arise from the mucosa of the uterus, and indicate catarrhal endometritis; these epithelia are found accompanied by ciliated pus-corpuscles, which arise from the epithelia. In freshly voided urine I have seen the cilia of both these formations in waving motion.

Common to Both Sexes. Flat epithelia of the bladder, in small numbers and without pus-corpuscles, are of normal occur-

rence in the urine. When present in a larger amount, together with pus-corpuscles and epithelia of the middle layers, exhibiting endogenous new formation of pus-corpuscles, they indicate acute catarrhal cystitis. The flat epithelia of the bladder may be found in clusters similar to those from the vagina; their size, however, is a sufficiently distinguishing feature. If the cuboidal epithelia largely outnumber the flat, or are scanty in comparison with the large amount of pus-corpuscles, the diagnosis of chronic cystitis is justified, and with greater certainty if some pus-corpuscles contain dark brown pigment-granules.

Caudate epithelia, somewhat smaller than those of the middle layers of the bladder, originate from the pelves of the kidneys. They are sometimes combined with clusters of uric acid crystals, which, when present in freshly passed urine, indicate their origin in the pelvis. Not infrequently these are accompanied by a large number of red blood-corpuscles and shreds of connective tissue, caused by hæmorrhage and ulceration in the pelves. Pelvic epithelia are often found in connection with kidney epithelia (pyelo-nephritis).

Small cuboidal and columnar epithelia are shed from the uriniferous tubules of the kidneys. They invariably indicate catarrhal nephritis, when pus-corpuscles are also present; with pus-corpuscles and tube-casts, they prove the presence of croupous nephritis. Without kidney epithelia in the urine, nephritis cannot be diagnosticated; these and the tube-casts are the only positive evidences of the presence of inflammation of the kidneys. In very acute nephritis, clusters—nay, cast-like tubes of kidney epithelia, may be found in the urine.

Tubular Casts. The most characteristic sign of croupous nephritis is the presence of tube-casts in the urine, and in my experience the casts are always indicative of the disease, and, with greater certainty, the larger the accompanying amount of the albumen. Reliable observers have seen casts without any albumen in the urine, and it has been asserted that mere hyperæmia of the kidneys may suffice to throw casts into the urine, without any evil consequences—for instance, after treatment with large doses of iodide of potash. The former assertion I can corroborate, the latter is not in concurrence with what I have seen; the casts surely indicate nephritis, and the greater their number the more serious is the disease.

We distinguish six varieties of tube-casts, viz.: hyaline, epithelial, blood, granular, fatty, and waxy casts. (See Figs. 367 and 368.) Their diagnostic value is as follows:

The *hyaline* and *epithelial casts*—not the desquamated epi-
ial tubes, but hyaline casts studded with epithelia—indicate
te croupous nephritis. They sometimes have a yellow color,
a slightly increased refracting power, owing to their imbibi-
of the coloring matter of the blood.

The *blood-casts* show hæmorrhage within the kidney; a larger
nber of such casts almost always foretells, more certainly in

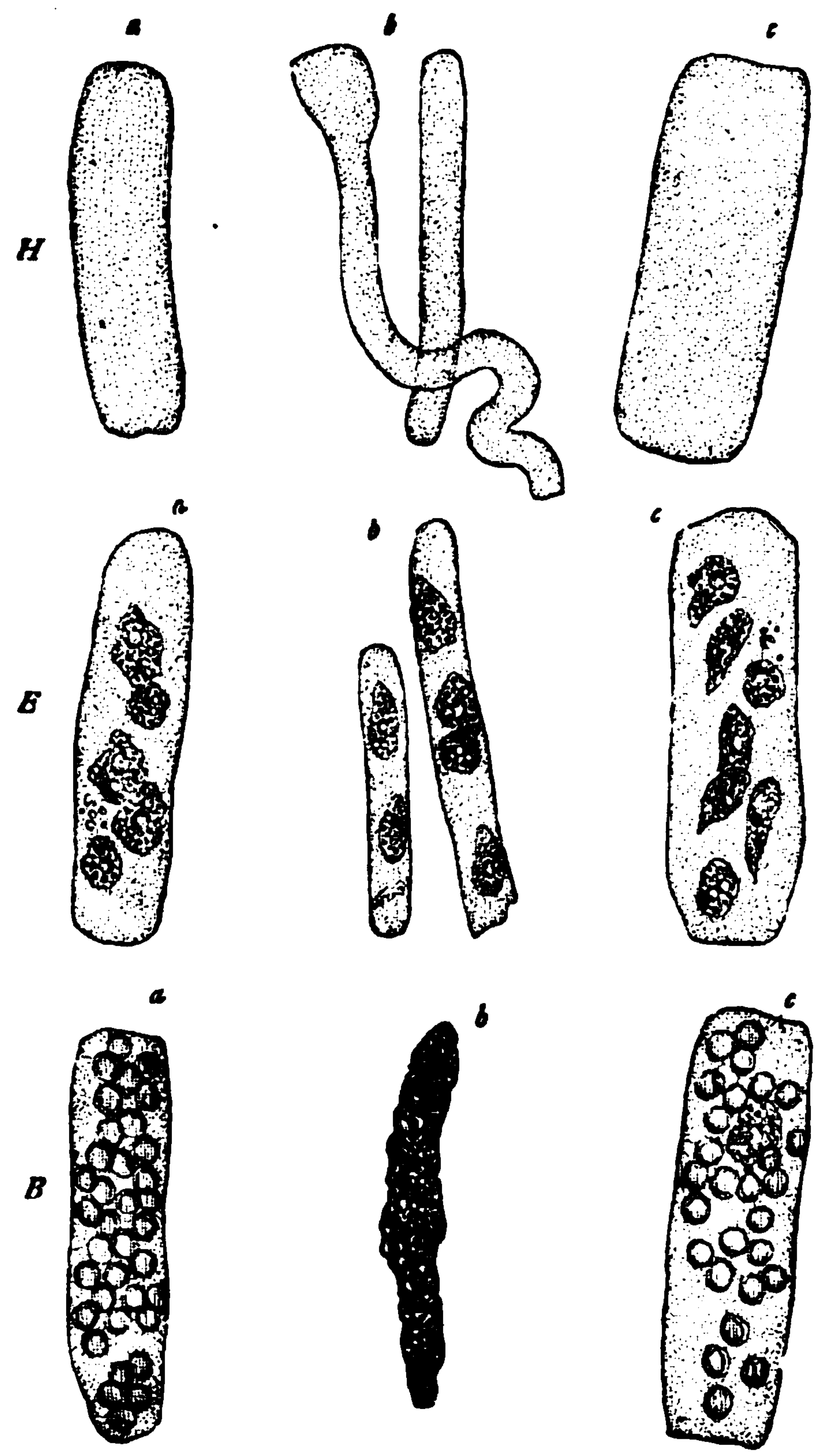

FIG. 367.—VARIETIES OF CASTS IN ACUTE CROUPOUS NEPHRITIS.

ie series *a* shows casts from convoluted tubules of the second order; the series *b*, casts the narrow portion of the loop-tubules; the series *c*, casts from the straight collecting es. *H*, hyaline casts; *E*, epithelial casts; *B*, blood-casts. Magnified 500 diameters.

lts than in children, fatal termination in a short period of
. If blood-casts have been retained in the tubules for some
, the blood-corpuscles lose their shape, and the cast has the
earance of a dark red-brown, granular cluster.

Granular, *fatty*, and *waxy casts* appear in the protracted,

chronic forms of croupous nephritis. The granular casts are probably due to the disintegration of the kidney epithelia and the lining endothelia; they, however, are seen sometimes also in acute croupous nephritis—especially in children after scarlet fever and diphtheria. Fatty casts indicate fatty degeneration of the kidneys, secondary to croupous nephritis. In all these

FIG. 368.—VARIETIES OF CASTS IN CHRONIC CROUPOUS NEPHRITIS.

The series *a* shows casts from convoluted tubules of the second order, the series *b*, casts from the narrow portion of the loop-tubules, the series *c*, casts from the straight collecting tubules. *G*, granular casts; *F*, fatty casts; *W*, waxy casts. Magnified 500 diameters.

instances the substance of the cast is the same, and only the outer adhering formations give the difference in the appearance.

Waxy casts are different in their chemical nature from hyaline casts, being characterized by a yellowish color, a great refracting power, wavy or fluted outlines, and a high degree of brittleness.

Such casts will not be seen — against the views of recent writers — unless waxy degeneration has been established in the kidneys.

Sometimes hyaline and epithelial casts exhibit spiral windings, probably from having originated in the spiral portion of the ascending branch of the loop-tubule. They have no special significance.

Besides, a great prognostic value attaches to the *size of the casts*. As a matter of course, casts formed in the convoluted tubules of the first order will never appear in the urine, as they cannot pass the narrow tubules. The mildest degrees of the disease are indicated by casts from the narrow tubules, the narrowest casts, and a small number of casts from the convoluted tubules. Not infrequently we meet with pedunculated casts, viz.: formations from the place of transition of the narrow tubules into convoluted tubules of the second order. Casts from the convoluted tubules justify the diagnosis of croupous nephritis in the cortical substance; casts of all the three sizes — the largest arising from the straight collecting tubules — permit of a conclusion of croupous nephritis in the whole organ, and upon this condition a very unfavorable prognosis can be established.

Based on these simple facts, I was enabled to give a prognosis, even where no danger was suspected by the attending physician. Dr. X., a prominent practitioner, brought me some fresh urine passed by his son, six years old, who had just recovered from a slight diphtheritic attack of the throat. The question was, whether in the fresh urine there could be seen moving micrococci and bacteria. I really found these low organisms, but, besides, also numerous tube-casts of all the three sizes. I told the father that his son was in danger. He laughed at me, and asserted that there was nothing from the clinical stand-point to justify such an alarming diagnosis. This happened on a Sunday, and I did not hear of the child until the next Wednesday, when I was informed that the boy had died in an uræmic fit. The physician now began to believe in microscopy, and a year afterward brought me some urine of his wife, containing a moderate quantity of albumen. In this urine I found fatty casts from the convoluted tubules, and, as the gentleman wanted to have a prognosis, I told him that his wife could not live longer than one or two years. In this case I was mistaken, as three months afterward the lady was carried away by uræmia.

Stress must be laid on the general constitution of the patient, such as can be positively recognized by the appearance of the pus-corpuscles present. We can tell how much the constitution had been lowered by the disease, and, of course, the prognosis will be the more unfavorable the more living matter the patient has lost — the worse, therefore, his constitution is at the time of examination.

Dr. R. E. Swinburne, in 1878, examined, in my laboratory, urine containing numerous casts, and both kidney epithelia and pus-corpuscles having very

little bioplasson, indicated a completely broken-down constitution. He diagnosed chronic croupous nephritis, and, when I inquired about the prognosis, he said, "The coffin ought to be made for the man." The next day the physician came who had brought the urine for examination, and, when he learned the diagnosis and prognosis, exclaimed, "Why, the man died last night; the coffin is being made for him."

Among the formations due to the presence of *entozoa* in the genito-urinary tract deserve to be mentioned: *hooklets of echinococci*, which, in rare cases, have been observed in the urine, indicative of the presence of ruptured sacs of the echinococcus in the kidneys. Further, the ova of the *distoma hæmatobium*, or *Bilharzia hæmatobia*, which are oval formations with a distinct shell and a short point at one pole. This entozoön lives in the veins of the prostate and the bladder, and by rupture of the vessels into the cavity of the bladder the ova are deposited in the urine. The disease occurs in North Africa only, and more especially in Egypt. I have, however, never seen formations of this kind myself. The *trichomonas vaginalis*, a ciliated animalcule living in the mucus of the vagina, is sometimes seen in the urine. In a case that came under my observation, the physician suspected an *ascaris lumbricoides* in the bladder of a child—the worm, as he supposed, having found its way through the urethra. Besides symptoms of acute cystitis, numerous dark brown granules were observed under the microscope, which perhaps might have been the fæces of the worm. Further particulars of the case were not known.

Diagnosis from Examination of Urine. Here I wish to briefly describe what, from my own observations, I have found to be correct. Whenever larger quantities of pus or blood are mixed with the urine, albumen is also present, and an approximate estimation must be made as to its amount, whether it is equal to that of the pus or blood present, or whether it exceeds the amount of the two latter. Expressions like "false albuminuria," or "pseudo-albuminuria," used for such cases, should be avoided, as no proper significance is attached to these terms.

Urethritis may be diagnosticated in the initial stages by the large amount of flat urethral epithelia; in later stages the pus-corpuscles are largely predominant, and cuboidal and columnar epithelia may also be seen. If long mucous cylinders are present, sometimes with knob-like terminations, which arise from the mucous glands of the urethra, the diagnosis *gleet* is justified. If, besides flat epithelia of the urethra, columnar epithelia, blood-

corpuscles, and shreds of connective tissue are found, *ulceration* and *stricture* may be suspected, more particularly if, in addition to the above-named formations, epithelia of the prostate make their appearance.

Prostatitis, occurring in young men subject to intense sexual excitement, and often mistaken for spermatorrhœa, may be diagnosticated by the presence of an increase of mucus, pus-corpuscles, and prostatic epithelia. After involuntary emissions of semen, spermatozoids are found in the urine. In all cases of so-called spermatorrhœa that have come under my observation, prostatitis was found to exist. In one case, the urine that was first passed from the urethra proved to be purulent, while the later portions were transparent; and many of the pus-corpuscles exhibited long cilia, as if a spermatozoid had been transformed into a pus-corpuscle. This feature rendered the diagnosis "suppurative inflammation of one vesicula spermatica" highly probable, and was in accordance with the clinical facts. Prostatic epithelia and prostatic concretions, together with the characteristics of cystitis, allow the conclusion of hypertrophy of the prostate.

Vaginitis is characterized by the presence of numerous vaginal epithelia, partly studded with micrococci and pus-corpuscles. The large cuboidal and columnar epithelia appear in the more intense degrees of vaginitis, and a large number of connective-tissue shreds are also found in ulcerative vaginitis. Mild forms of vaginitis are observed in almost all women suffering from endometritis, more particularly after the delivery of children. Vaginal epithelia may be completely absent in the urine of small girls and virgin matrons.

Cervicitis may be diagnosticated by the presence of cervical epithelia and pus-corpuscles; ulcerative cervicitis is marked by the shreds of connective tissue, in addition to the usual epithelia and pus-corpuscles.

Endometritis shows in the urine ciliated columnar epithelia of the mucosa of the uterus and ciliated pus-corpuscles arising from them. Ulcerations are marked by the presence of shreds of connective tissue and blood. How far the diagnosis of tumors of the uterus is admissible from the examination of urine, I am unable to tell from my own experience.

Cystitis may be recognized both in its acute and chronic stages. In *acute* cystitis the urine may be acid, containing a varying amount of pus-corpuscles and epithelia from upper and middle layers of the bladder, the latter exhibiting the character-

istic features of endogenous new formation of pus-corpuscles. In subacute cystitis the features are similar. In *chronic catarrhal cystitis* the flat epithelia of the bladder are usually absent, and only those of the middle and deepest layer (cuboidal and columnar) found. In chronic cystitis the pus-corpuscles sometimes contain dark-brown granules of pigment. In the highest degrees of cystitis scarcely any epithelia are present, and only enormous quantities of pus-corpuscles, mostly swelled, hydropic and disintegrated, are to be seen. The urine being highly alkaline, the purulent sediment produces a jelly-like, viscid mass, in which, besides crystals of alkaline salts, clusters of micrococci are present. The presence of blood-corpuscles and shreds of connective tissue, in addition to the other features, indicates ulcerative cystitis. Large quantities of blood may entirely conceal the original inflammatory trouble.

Villous Tumors of the bladder yield large shreds of tissue, sometimes containing capillary blood-vessels choked with blood. Occasionally fibrinuria temporarily accompanies villous tumors. (Hofmann and Ultzmann).

Pyelitis may be recognized by the presence of pelvic epithelia and pus-corpuscles. Epithelia from the pelvis of the kidney and blood-corpuscles are found in pelvic hæmorrhage. The urine in this affection is distinctly acid and laden with uric acid, which, as the so-called gravel, is observed in the freshly passed urine. Ulcerative pyelitis may be recognized by the additional presence of shreds of connective tissue. The pelvic epithelia being in fatty degeneration, chronic pyelitis may be recognized.

Hæmorrhage from the kidneys is marked by the presence in the urine of kidney epithelia, red blood-corpuscles, and delicate shreds of connective tissue; these are all of a yellow hue, from the coloring matter of the blood.

The diagnosis of *catarrhal nephritis* may be made when pus-corpuscles and kidney epithelia are voided, the presence of columnar epithelia from the straight collecting tubules indicating an invasion of the pyramidal substance. In *acute catarrhal nephritis* both the kidney epithelia and pus-corpuscles are numerous; albumen may be present in a varying quantity, but not infrequently it is absent during the whole course of the disease. Small numbers of hyaline casts, mainly from the narrow tubules, and red blood-corpuscles, at times accompany the previously named formations.

In *subacute catarrhal nephritis* all features may at times be

absent, at other times present in varying numbers. In *chronic catarrhal nephritis* and its termination, the *cirrhosis of the kidneys*, the patient voids large quantities of a pale, watery urine, in which few or no salts are to be found; this condition will be more marked the farther the stage of shrinkage has advanced. Albumen at times is present in small quantities, at times absent. The few kidney epithelia and pus-corpuscles are the only reliable features for diagnosis; sometimes these are accompanied by small shreds of connective tissue. If the kidney epithelia and pus-corpuscles are finely granular and disintegrated to any great extent, the approaching end of life may be foretold.

Croupous Nephritis. All the features of catarrhal nephritis are present, with the addition of casts. The nature of the casts allows us to decide whether acute or chronic croupous nephritis is present. In both instances the amount of albumen is great, and is found to be still more abundant if blood is mixed with the urine. The amount of albumen, the number of the casts and their sizes, determine the intensity of the inflammatory process. The prognosis is more unfavorable in adults than in children.

If casts characteristic of chronic croupous nephritis are mixed with casts such as we find in acute croupous nephritis, the diagnosis of a chronic inflammation with acute recurrence, *i. e.*, of subacute croupous nephritis, can be made. The presence of clusters of delicate fat-granules entangled with the albumen (if coagulated by the addition of chromic acid) indicates fatty degeneration of the kidney, the more certainly if fatty casts are also met with. Waxy degeneration can be diagnosticated both from the waxy metamorphosis of the shed-off kidney epithelia and the presence of waxy casts. Cases of the recovery of children even from such a disease are on record. In slowly running cases of chronic croupous nephritis the prognosis rests upon the general constitution of the patient, as determined mainly by the condition of the pus-corpuscles.

Suppurative nephritis exhibits all the features of acute croupous nephritis, with the addition of very large quantities of pus-corpuscles. A ruptured abscess of the kidney may be recognized if, besides numerous pus-corpuscles, numbers of kidney epithelia and shreds of connective tissue are also found. The presence of hæmatoidin crystals would point toward the chronic course of the abscess, which may have existed for some time previous to its evacuation, and which, after bursting, may, for weeks or months, continue discharging pus.

XXI.

THE MALE GENITAL TRACT.

THE male genital organs are: first, the *testes*, which are destined to produce the fructifying principle of reproduction, the *semen* or *sperm*; second, the *vas deferens and seminiferous vesicles*, whose office is to carry and store it up; and third, the *penis*, for transferring the spermatic fluid into the female genital organs. The prostatic and Cowper's glands are accessory organs, which produce mucus mainly. The *spermatozoids* are the essential fructifying element of semen. These are bioplasson formations, varying greatly in size and shape in different animals. In man they are pin-shaped, with a thickened head and a thread-like tail, which at its point of attachment to the head is slightly conical, exhibiting either a pear-shaped, a knob-like, or a double lobate enlargement. The head is of a roundish, ovoid, or conical shape, the point representing the free proximal end. Their length is, on an average 0.0040 mm. Sometimes the whole formation appears homogeneous, and of a high luster. Sometimes a vacuole is observed in the head, and sometimes a delicate reticular structure can be traced throughout the thickened portions. Spermatozoids, when in a fresh condition, are in an active winding or spiral motion, executed by the tail, through which motion the head is rotated with a boring movement, and at the same time the spermatozoid changes its place. This motion is favored by slightly alkaline media, dilute solutions of table-salt, and of phosphate of soda; acids, on the contrary, soon produce rest.

Spermatozoids retain their shape after having lost their mobility for a long while, even after they have been allowed

to dry; and they are peculiarly resistant to the action of acids and alkalies. In the vas deferens they are motionless, there being but little liquid present. Upon the admixture of mucus (from the prostate) the spermatozoids at once assume a high degree of activity.

(1) The *testes* are compound tubular glands. The seminiferous tubules, originally very numerous, by repeated union become fewer, and at last collect into one large tubule—the vas deferens. The fibrous connective tissue coat, ensheathing the whole organ (tunica albuginea), sends prolongations carrying the blood-vessels between the tubuli; broader septa of connective tissue are also present, producing an indistinctly lobular structure in the testes;

A

E

C

E

FIG. 369.—TESTIS OF ADULT.

A, tunica albuginea; *V*, blood vessel, *C*, connective-tissue frame, carrying blood-vessels, and *E*, *E*, rows of coarsely granular plastids, *TS*, transverse section of seminiferous tubule, *OS*, oblique section of seminiferous tubule. Magnified 200 diameters.

at their upper posterior aspect, in the corpus Highmori, the septa are most developed and inclose sinuous spaces. The blood-vessels are most numerous in the inner portions of the albuginea; its smooth, external surface is covered with flat endothelia, which continue into the so-called serous sheath of the testes. The connective tissue between the tubules, besides the ordinary connective-tissue corpuscles, holds a varying number of coarsely granular plastids, which are often arranged in rows, exhibiting a brownish

color resembling tubular epithelia. Their significance is not understood. (See Fig. 369.)

The seminiferous tubules show three marked divisions, which are: the convoluted, the straight portion, and the rete testis. The convoluted tubules compose the main mass of the testis, and at the periphery unite and form a continuous closed net-work having a few offshoots with blind terminations (Mihalkovics.) By continuous union at acute angles their number decreases toward the corpus Highmori; they gradually become less convoluted, and continue until, with an abrupt narrowing, they pass into the straight portion. The caliber of the straight tubules is about one-third the size of the convoluted. These tubules are imbedded in a broad connective-tissue layer, and inosculate with the rete testis, which forms a dense, narrow, and sinuous net-work of tubules, occupying the spaces of the corpus Highmori. From this net-work arise the efferent vessels of the epididymis.

The convoluted tubules have a lining of irregular cuboidal epithelia, arranged in several layers. The outermost layer is, as a rule, composed of coarsely granular elements, while the inner layers are in the condition of rest, either uniformly distributed or arranged in rows irregularly projecting toward the central caliber. In the condition of rest the caliber is found either empty or filled with an albuminous liquid, which, in specimens hardened in chromic acid, appears finely granular. In some tubules no trace of spermatozoids can be discerned; in others, especially in men who have died of chronic wasting diseases, the spermatozoids are scanty; other tubules, on the contrary, are entirely filled with epithelia, and their offspring the spermatozoids. In the rat's testis, and in all animals during the rutting period, the spermatozoids are in most portions of the convoluted tubules so numerous that their tails fill the central caliber, showing a spiral, sheave-like arrangement. (See Fig. 370.)

The connective-tissue layer next to the epithelia (the membrana propria) is composed of a number of delicate strata, which, according to Mihalkovics, are composed of a number of closely packed, flat endotholia, their nuclei being traceable in a more or less homogeneous, elastic basis-substance.

Regarding the formation of spermatozoids, the views of investigators differ widely; some claiming that only certain epithelia, the so-called spermatoblasts, participate in the formation of the spermatozoids, while other epithelia produce mucus

only. My own observations prove that the radiating rows of epithelia coalesce into continuous masses, in the most peripheral portions of which the heads of the spermatozoids are produced, while the tails are formed by the more central parts.

The steps in the formation of spermatozoids are as follows: The epithelia nearest the connective tissue become coarsely granular, and in part nucleated; next we see enlarged epithelia, in which the bioplasson assumes irregular, rod-like forms, arranged without much regularity. Then follows a layer composed of coalesced epithelia, the bioplasson of which has grown into bulky formations, which are the heads of the spermatozoids, while the rods in the central portions of the rows become parallel, and coalesce to form the tails. Around the spermatozoids numbers of unchanged bioplasson-granules are seen, and the

FIG. 370.—TESTIS OF A RAT.

C, connective-tissue sheath, producing septa between the seminiferous tubules, in which course the blood-vessels *F*. *E*, rows of epithelia of the seminiferous tubules; *S*, tails of spermatozoids, filling the caliber of the tubule. Magnified 200 diameters.

first-formed spermatozoids are studded with these granules. As the liquefaction of the unchanged bioplasson—*i. e.*, the formation of mucus—proceeds, the tails appear smooth and without any attached granules. Coarsely granular plastids, in limited numbers, are left unchanged, and mixed with the completed sperm. (See Fig. 371.)

The epithelia of the straight seminiferous tubules are columnar; those of the plexus, within the corpus Highmori, are flat. Neither of these take any part in the formation of spermatozoids.

Blood-vessels are numerous in the testis, the capillaries producing a reticulum around the seminiferous tubules. A closed reticulum of lymphatics, twining around the tubules, has been known since His, Kölliker, and others.

The Terminations of the Nerves in the Testicle.

By H. G. Beyer, M. D., M. R. C. S., Passed Assistant Surgeon, U. S. N.*

The only observations on the terminations of the nerves within the seminiferous tubules at present on record, are those of Letzerich.† He uses either fresh seminiferous tubules, or such as have been in a solution of very dilute chromic acid for the period of twenty-four hours; then he teases them out carefully with needles, and examines them under the microscope. Under "favorable circumstances," he finds that the nerves approach the membrana propria, perforate the same, and finally terminate in granular masses or knobs between the latter membrane and the first layer of cells. I must say that circumstances never favored me in finding the structures pictured in the plates accompanying his article. In this I have been no less unfortunate than Von La Valette St. George.‡

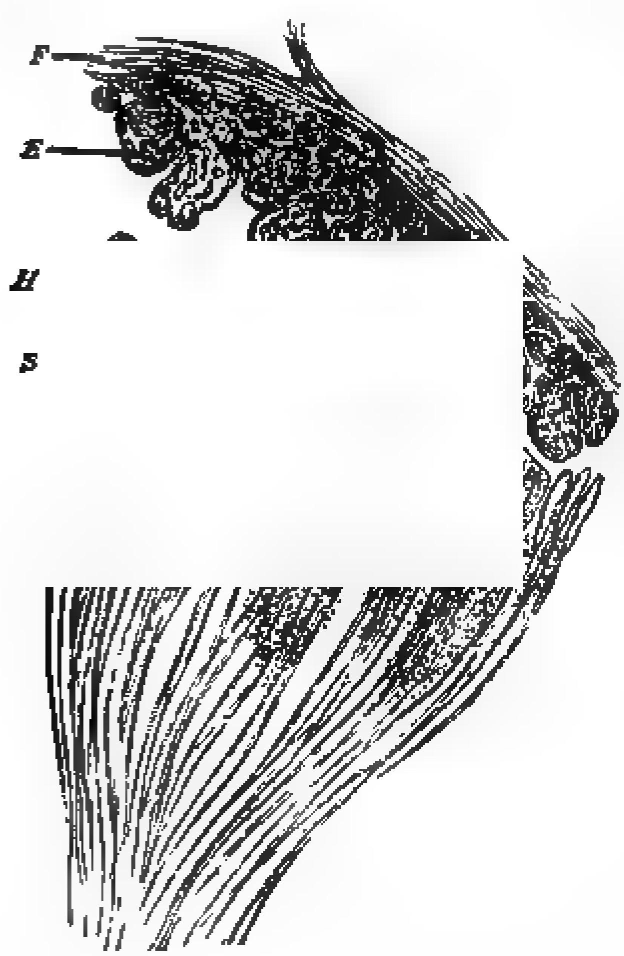

Fig. 371.—Testis of Rat.

F, connective-tissue frame; *E*, irregular cuboidal epithelia, with rod-like formations of bioplasson; *H*, epithelium, in which the rods have assumed the shape of heads of spermatozoids; *S*, spermatozoids sprung from coalesced rows of epithelia, some of which have furnished the heads, others the tails, of the spermatozoids. Magnified 600 diameters.

The methods of investigation followed out in my researches require a brief notice. The testicles used were those of the dog, calf, mouse, rat, rooster, and man. Both teasing and section-cutting were praticed; the former method, however, I found quite superfluous. The tissues from which the material for study was collected were both fresh and hardened, the hardening being done by alcohol, chromic or picric acid. The staining agents which I found of most advantage were chloride of gold, osmic acid, picro-carmine, and eosin with logwood. For the study of the nerve-fibers outside the seminiferous tubules, and their plexuses around the tubules arising from the larger nerve-bundles which pass along the small arterioles, osmic acid and picro-carmine have, in

* Printed in abstract from the author's manuscript. † "Virchow's Archiv." Bd. 42.
‡ "Stricker's Handbook of Histology."

my hands, given good results. I can also recommend eosin with logwood for the same purpose, as deserving a trial.

The chloride of gold method is still the only available one for bringing out the ultimate nerve-terminations. Some of the most beautiful and convincing specimens in my possession are sections of the testicles of young rats, which were hardened in chromic acid and then stained with chloride of gold, in strict accordance with the rules laid down by Cohnheim. Such specimens will show improvement during the first twelve months. It was certainly a step in advance when Löwitt introduced his formic acid method, by which we are enabled to allow the reduction of gold to take place in a darkened bottle. This method, in some cases, gives better and more uniform results, and reduces the metallic precipitate, so often found on the surface of sections, to a minimum; but the destruction of the epithelia which this process entails is not in all cases desirable.

In hardening, staining and preparing tissues generally, I have preferred to cut up the testicles into sections of from two to three millimeters in thickness, and, instead of the imbedding methods, I found it much more convenient to use the freezing microtome for fine sections. In so doing two things are avoided — viz.: shrinkage and the introduction of foreign material.

Being obliged to use high powers for the recognition of the ultimate termination of the axis-fibrillæ, the thinnest sections were chosen and mounted in glycerine to which one-third of its volume of distilled water had been added. Specimens stained with osmic acid and picro-carmine can be advantageously treated after the plan proposed by E. Neumann, which is that of temporarily mounting in glycerine mixed with muriatic acid in the proportion of two hundred parts of the former to one of the latter, and carefully watching until the orange-red coloration has been reduced to the nucleus, then washing out thoroughly in distilled water.

Anatomists agree that the nerves of the testicle are derived from the sympathetic. As long ago as 1834, Joseph Swan * gave a very good representation of the spermatic plexus of nerves. According to Robert B. Todd,† the nerves of the testicle are derived chiefly from the renal plexus, but partly also from the superior mesenteric and aortic plexuses. These nerves then descend in company with the spermatic artery to the cord, where, being joined by branches from the hypogastric plexus which passes along the vas deferens, they form together the sperm-plexus. The branches of this plexus are intermingled with the vessels of the cord, and ultimately terminate within the substance of the testis. A few twigs may also be traced to the coverings of the gland. Sappey ‡ recognizes two sources of nerve-supply, namely, one from the plexus accompanying the spermatic artery, which, he says, alone penetrates into the substance of the testis, and the other from the plexus surrounding the vas deferens, which, according to his view, terminates in the epididymis.

In regard to the nerves running within the structure of the testis, I can corroborate the views above detailed, namely, that none but non-medullated nerve-fibers are found; and I can add that their characteristic arrangement is in the shape of plexuses. These, when found in the neighborhood of the larger arterioles, are, of course, large in proportion. As they pass on, always

* "A Demonstration of the Nerves of the Human Body," London, Plate V.

† "Cyclopedia of Anatomy and Physiology," vol. iv., pt. 2, pp. 982.

‡ "Anatomie Descriptive," tome 4, p. 614.

accompanying the blood-vessels, they, by division and frequent branching, become more numerous and very much smaller, until finally, after having reached the capillaries, they are extremely thin and transparent, and almost escape the observer's eye in the fresh and unstained specimen. In successful sections, however, they can still be observed to preserve the plexiform arrangement. When found in the proximity of a seminiferous tubule, they are generally situated between a capillary and the basement-membrane. As they penetrate this membrane, the nerve-fibers, still including several axis-cylinders, break up into their ultimate fibrillæ, at first pass along between the several layers of endothelia of which the basement-membrane is composed, and, after having emerged from its inner wall, they, as it were, line its interior with a plexus consisting of the ultimate axis-fibrillæ, being interrupted only by variously shaped bodies, most of which present a pyramidal shape. This plexus thus lining the inner surface of a seminiferous tubule is best observed in the testicles of animals in which the membrana propria is very thin and is composed of but one layer of endothelia, such as the mouse and the rat. From this plexus, best seen in gold preparations, viz.: longitudinal sections which have lost most of their epithelium, so as to expose the inner surface of the seminiferous tubule, the axis-fibrillæ pass upward at acute angles in a direction toward the center of the tubule. Between the epithelia superimposed upon the membrana propria, the fibrillæ anastomose in every direction, and hold, so to say, the epithelia in a mesh-work. The best and most clearly defined pictures are represented in specimens of the testicle of the young rat.

The cement-substance between the epithelia is the plan of the ultimate termination of the axis-fibrilla in the testicle.

I have never seen a nerve-fiber penetrate into the interior of an epithelium, although it might seem so when one of them crosses an epithelium and is interrupted in its course.

The ultimate axis-fibrillæ, having been traced traversing the cement-substance between the epithelia, and being connected with the filaments or prickles crossing them, we are at once in a position to understand how the function of the epithelia within the seminiferous tubules — viz.: the production of spermatozoids — is under the direct control of the sympathetic system.

(2) The *epididymis* is composed of a single tubule with numerous convolutions, with which the seminiferous tubules unite after leaving the corpus Highmori, and producing the convoluted coni vasculosi. These tubules are now termed efferent. They all have a circular coat of smooth muscle-fibers, external to the membrana propria. The epithelia are columnar, ciliated, numerous smaller, wedged plastids being present between their pointed feet. Toward the cauda epididymidis the wall of the efferent vessel increases in thickness, and is supplied with longitudinal muscle-bundles. A delicate, adventitial connective tissue, rich in elastic fibers, supports the convolutions of the tubule of the epididymis, being rich in capillary blood- and lymph-vessels. These circulate through the adventitial coat, penetrate the muscle-layer, and produce a terminal capillary plexus above the epithelia.

(3) The *vas deferens* has a broad wall, which is composed mainly of three layers of smooth muscle-fibers—an inner and outer longitudinal and a middle circular layer. (See Fig. 372.)

The most internal mucous layer, when the tubule is empty, is arranged in folds, and covered with a single layer of columnar epithelia. The only vas deferens which I have examined exhibited ciliated columnar epithelium; all authors claim, however, that cilia are not present. The bundles of the longitudinal muscle-layers are loosely arranged, and freely intermixed with fibrous connective tissue abundantly furnished with elastic fibers,

FIG. 372.—VAS DEFERENS. TRANSVERSE SECTION.

E, folds of the mucosa, covered with columnar epithelia, *M*, mucous layer, composed of delicate bundles of connective tissue, C^1, inner longitudinal, C_2, outer longitudinal, layer of bundles of smooth muscle-fibers, freely intermixed with connective tissue; *T*, circular muscle-layer; *O*, adventitial connective tissue, carrying the larger blood-vessels. Magnified 100 diameters.

while in the circular layer the muscle-bundles are arranged more closely. The most external layer is composed of loose, fibrous connective tissue, rich in blood-vessels, lymphatics, and nerves.

(4) The *ampulla* of the vas deferens and the *seminal vesicles* have walls considerably thinner than those of the vas deferens proper. In the ampulla the mucosa has abrupt folds, and the

lining columnar epithelium sends prolongations into the connective tissue—the glandular nature of which is not generally agreed upon, as some observers claim these formations to be merely sinuosities of the mucosa. The epithelia contain a varying number of brown pigment-granules. Three layers of smooth muscle-fibers are discernible. Similar structures are found in the walls of the seminal vesicles. The *ejaculatory ducts* are covered with ciliated columnar epithelia (authors do not mention the cilia), and the muscle-layers are said to be only an inner longitudinal and an outer circular. Toward the opening at the summit of the seminal hill, the epithelia gradually change into a stratified formation composed of several layers. In this situation the mucosa has numerous sinuous veins, agreeing with the general structure of the male urethra.

(5) As *remnants of embryonal formations* are considered:

The *paradidymis* (Giraldès), which consists of single or multiple lobules at the vascular porta of the testis, between the blood-vessels of the spermatic cord; each lobule being composed of convoluted tubules, with a blind termination, and lined with ciliated columnar epithelia. It is considered to be a remnant of the primordial kidney (Wolff's body), being homologous with the parovary of the female.

The *vas aberrans Halleri* and the *vasa aberrantia* of the *rete testis* (M. Roth) are blind tubules, kindred in structure to the tubule of the epididymis and the tubules in the corpus Highmori. Both are remnants of the genital portion of Wolff's body.

The *hydatid of Morgagni* is a non-pediculated lobule at the anterior aspect of the testis, immediately in front of the head of the globe. It is composed of vascularized connective tissue, and covered with ciliated epithelia, which, according to E. Fleischl, send prolongations into the depth of the hydatid. The center holds a canal, which is lined with ciliated epithelia; this canal may be widened into a vesicle, and, if in communication with the tubule of the epididymis, is found filled with semen (Luschka). It is considered as an analogy of the ovary.

The *pedunculated hydatid* is not constant; it is a vesicle the size of a millet-seed, attached to the head of the epididymis by means of a slender pedicle. It is a remnant of the embryonal Müller's duct (Krause).

(6) The *prostate gland* surrounds the initial portion of the male urethra, mainly at its posterior and lateral circumference. It is composed of acinous glands, which exhibit numerous convolutions, and are lined with cuboidal epithelia in several layers. The acini are sometimes small in comparison with the large ducts, which are lined with columnar epithelia; sometimes the acini are imperfectly developed, and the ducts seem to represent chiefly the glandular structure. In the acini, not infre-

quently, peculiar, concentrically striated colloid corpuscles of a high luster are observed—the so-called prostatic concretions.

According to Langerhans, the epithelia of the gland are arranged in two layers, the superficial being conical and elongated, the deeper globular; Toldt maintains having seen this arrangement in one prostate gland, while in three others which he studied only one layer of columnar epithelia was present. There seem to be varieties in the arrangement of the glandular epithelia. The interstitial tissue is scantily supplied with connective tissue, but plentifully with smooth muscle-fibers, which are arranged without any apparent regularity. At the periphery of the prostate gland the muscle-bundles coalesce, forming continuous layers, and in this situation are freely intermixed with

FIG. 373.—PROSTATE GLAND OF AN ADULT.

M, interstitial connective tissue, rich in bundles of smooth muscle-fibers. *F*, cuboidal epithelia, lining the convoluted acini. *C*, prostatic concretions. Magnified 200 diameters.

striped muscles, which surround the gland. The smooth muscle-layers are continuous with the circular sphincter muscles of the bladder.

(7) *Cowper's glands* are acinous glands, with irregular sinuosities and stratified cuboidal epithelia. The lobules of these glands are separated from each other by dense fibrous connective tissue, which is traversed at the peripheral portions by bundles

of striped muscle-fibers of the perineal tract. Sometimes the lobules are separated by the intervening connective and muscle-tissues.

(8) The *penis* consists of two cavernous bodies, which in their under furrow hold the urethra, surrounded by a cavernous body of its own. The cavernous body is composed of trabeculæ of dense connective tissue, rich in smooth muscle-fibers, capillary blood-vessels, and medullated nerves. (See Fig. 374.)

The trabeculæ inclose venous sinuses, and at the boundary surface are lined with flat endothelia. These sinuous spaces are coarsest in the cavernous bodies of the penis, somewhat smaller in the glans, and smallest in the cavernous body of the urethra. According to C. Langer, the arteries which supply the cavernous

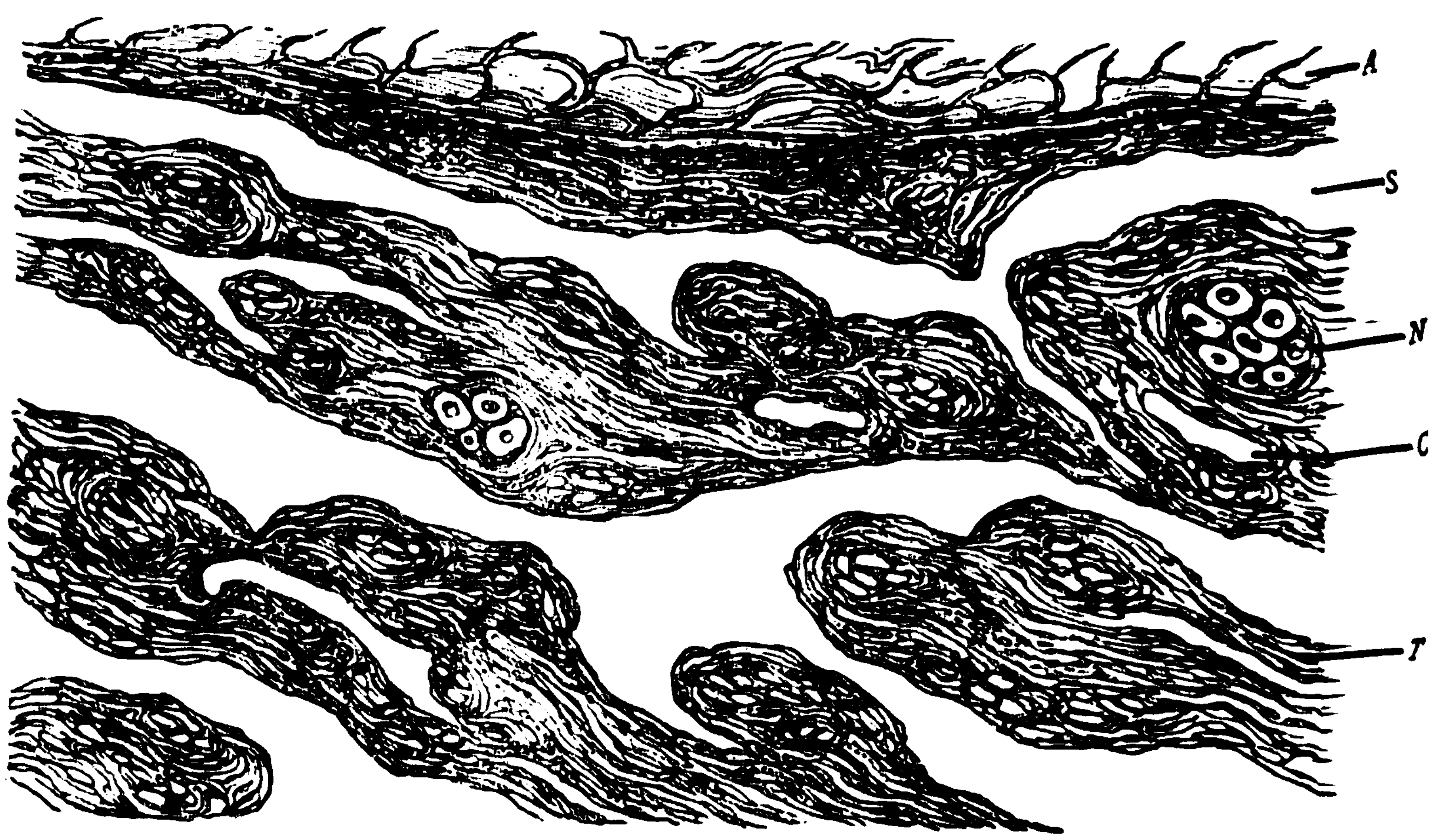

FIG. 374.—CAVERNOUS BODY OF THE PENIS. TRANSVERSE SECTION.

A, tunica albuginea; *S*, venous sinuses; *T*, trabeculæ of connective tissue, holding capillary blood-vessels *C*, and bundles of medullated nerve-fibers *N*. Magnified 200 diameters.

bodies are marked by a broad muscular coat, and they anastomose freely within the trabeculæ. Some of them empty directly into the sinuses of the cavernous body, and others divide into capillaries which run below the albuginea and along the septum, producing a delicate reticulum which inosculates with the venous sinuses, and are the main source of blood-supply to the latter. The sinuses are smaller at the periphery than in the center of the cavernous bodies. It is an unsettled question whether the capillaries of the trabeculæ themselves, which produce a wider mesh-work than those at the periphery,

also empty into the venous sinuses. The before-named observer and Rouget have demonstrated that the so-called arteriæ helicinæ, which take a spiral course, and are found mostly in the posterior portions of the corpora cavernosa, are only the loops of arteries visible in the collapsed condition of the penis, and which have no cecal terminations, as former anatomists thought. Nevertheless, Henle maintains the existence of helicine—blind vessels—and considers them as a sort of glandular apparatus. The efferent veins collect on the upper and under surface of the penis, uniting mainly in the vena dorsalis penis; those of the under surface receive the blood from the large cavernous sinuses. The inner surface of all these veins is richly provided with ledge-like, branching projections, which are composed of smooth muscle-fibers; free trabeculæ of a similar structure also traverse the calibers of the veins.

XXII.

THE FEMALE GENITAL TRACT.

THE female genital organs are: first, the *ovaries*, whose office is to produce the essential principle of reproduction—*i. e.*, the ovum; second, the *uterus*, to retain the fructified ovum during the period of development; and third, the *vagina*, to receive the seminal fluid of the male for fructification. The organ, upon which reproduction mainly depends, is the *ovum*. The mature human ovum is a globular vesicle of an average diameter of 0.200 mm., inclosed by a cuticular sheath — the *zona pellucida*—in which delicate radiating striations are seen. In the ova of many animals the cuticle is known to be perforated by an opening — the *micropyle*— to admit the entrance of the spermatozoids. The ovum contains granules which are partly minute, partly coarse, representing the yolk, and also an eccentrically situated, nucleus-like formation — the *vesicula germinativa*—the bioplasson of which is distinctly reticular, holding in its center a somewhat coarser granule — the *macula germinativa*.

The matured ovum is discharged from the ovary a few days before the beginning of menstruation. It is carried by the Fallopian tube into the cavity of the uterus, and in any locality, after leaving the ovarian follicle, may be reached by the spermatozoids. The number of the spermatozoids which penetrate the ovum is known to vary greatly, although, perhaps, a single spermatozoid is sufficient for the impregnation of the ovum. As regards the determination of the sex, all observers since Aristotle's time point toward the fact that the sex of the future being is determined in the moment when impregnation takes place. Careful observations of stock-farmers and of physicians in lying-in hospitals have settled the fact that, when coition takes place shortly before the appearance of menstruation, or in animals at the begin-

ning of heat, the offspring is a female. If, on the contrary, impregnation occurs shortly after menstruation, or in animals toward the end of the rutting period, a male is the result. Based upon these facts, the following hypothesis is admissible: Before menstruation the ovum, being high up in the female genital tract, can be reached by a few spermatozoids only; while, after menstruation, the ovum lying in the lower part of the uterine cavity, can after coitus be reached by a larger number of spermatozoids. The ovum is a formation of living matter of the female, the spermatozoid a formation of living matter of the male. Both have plastidules representative of the organism *in toto*; and if after commingling the living matter of the female be in excess, only one or a few spermatozoids having entered the ovum, a female organism will be produced. Should, on the contrary, many spermatozoids have entered the ovum, the living matter of the father will predominate over that of the mother, and the result will be a male organism. This hypothesis may sustain the idea that the sex of the future individual is determined in the moment of impregnation; it also agrees with the fact that peculiar bodily or mental properties of the father are, in the majority of cases, transferred to the male offspring, while bodily and mental properties of the mother usually reappear in the female children, though all these characteristics may, in varying proportions, be present in either sex, since every new being is the result of a mixture of male and female living matter. Exceptionally, however, characteristics peculiar to the father, f. i., a hare-lip, reappear in the female offspring exclusively, for which fact the above hypothesis offers no satisfactory explanation. Neither can it be understood how, in some insects (f. i., bees), male offspring are produced independently of the male—*i. e.*, without sexual intercourse. This strange peculiarity, to which Sieboldt first drew attention, cannot be understood by any theory yet advanced, and we must rest satisfied for its designation with the Greek word "parthenogenesis."

(1) *The Ovary.* The essential characteristics of the ovary are its epithelia, which Waldeyer terms the "*germinal epithelium.*" This observer discovered that the peritoneum produces no cover for the ovary, but terminates with a jagged border at the hilus of this organ. The surface of the ovary, at all periods of life, is covered by one layer of columnar or cuboidal epithelia; these are the remains of the germinal epithelium which gives origin, in the earliest stages of embryonal development, to all glandular formations of the genito-urinary tract. Among the germinal columnar epithelia Waldeyer found larger epithelia of a globular shape, with a large, sharply defined nucleus, which, according to him, are developed into ova. My own researches, though limited, point toward the conception that the ovum is the product, not of a single epithelium, but of quite a number of them, which by coalescence at first produce multinuclear bodies, and later exhibit only one larger central nucleus as a secondary formation.

All glandular formations of the ovary arise, according to

Waldeyer, from a proliferation of the germinal epithelia, which is accompanied by an outgrowth of connective tissue from the center toward the periphery. The germinal epithelia produce prolongations in the shape of tubules or solid strings, which at first are connected, holding in their centers rows of larger nucleated epithelia—the "ovular chains" of Pflüger. At the time of birth, such cord-like formations, in a plexiform arrangement, are still recognizable, though, in the depth of the organ, numerous epithelial groups appear already isolated by surrounding connective tissue, being, at this stage, termed the *follicles of the ovary*. Each follicle is a globular formation, composed of a single lining row of short, columnar epithelia, surrounding a finely granular, central, nucleated body—the ovum. In more advanced stages of development the connection between the surface epithelium and the epithelial follicles disappears, and each follicle is surrounded and enclosed by its own layer of connective tissue. Exceptionally, two ova are observed in one follicle.

As development progresses, numerous layers of cuboidal epithelia are gradually formed within the follicle, and only the layer nearest the wall of the follicle and the layer lying close around the ovum retain their columnar character. The row of columnar epithelia immediately surrounding the ovum is termed the *zona granulosa* or *radiata*; between this and the ovum proper—which, as before mentioned, is also epithelial in nature—a broad, cuticular formation is developed—the *zona pellucida*. Numerous cuboidal epithelia are transformed into a mucous mass, which is subsequently changed by liquefaction into what is termed the *follicular liquid*. Traversing the cavity of the follicle, comparatively few epithelial strings are left of an irregular shape. The ovum, approaching its maturity, is either suspended by such epithelial strings or remains attached to the wall of the follicle, usually opposite the pole of the follicle which looks toward the periphery of the ovary. (See Fig. 375.)

With advancing growth the follicle—called Graafian follicle—becomes easily discerned with the naked eye, and exhibits a distinct layer of inclosing fibrous connective tissue,—the *theca folliculi*,—which is in continuity with the connective-tissue stroma of the ovary, and shows an ample supply of capillary blood-vessels. Between the theca and the adjacent columnar epithelia lining the follicle a marked basement- or elastic layer may be observed. The point where the follicular epithelium is accumulated around the ovum bears the name of the *proligerous*

disk, which protrudes more or less toward the central cavity. Near the time of maturity of the ovum, the epithelia of the follicle opposite the disk are destroyed, the connective tissue around the follicle is deprived of its blood-vessels, and this thinned portion ruptures; the follicle empties its liquid, and the ovum is discharged, still surrounded by a layer of columnar epithelia—the *zona granulosa* or *radiata* of authors.

After the follicle has emptied, a slight hæmorrhage takes place at the site of the former cavity. The extravasated blood leaves a certain amount of pigment behind, and the newly ap-

FIG. 375.—FOLLICLE OF THE OVARY OF A RABBIT.

C, dense connective tissue—so-called capsule of ovary; *T*, fibrous connective tissue—the stroma of the ovary, *E*, stratified lining epithelium of the follicle; *S*, epithelial strings traversing the cavity of the follicle, *L*, albuminous liquid filling the cavity of the follicle, *ZG*, zona granulosa, composed of columnar epithelia; *ZP*, zona pellucida—a cuticular formation; *O*, ovum with the vesicula germinativa. Magnified 200 diameters.

pearing medullary corpuscles, both from the connective tissue and the epithelia of the follicle, appear laden with pigment-particles, or saturated by a diffuse coloring matter. At a certain period a number of pigmented medullary or inflammatory corpuscles appear in the part where the former follicle was situated; these are more numerous and more laden with pigment when

the discharged ovum is impregnated and the rupture of the follicle followed by pregnancy. The difference between a *false corpus luteum* (after menstruation) and a *true corpus luteum* (after pregnancy) consists only in the number of medullary corpuscles and the amount of pigment present. The coloring matter has the characteristics of hæmatoidin, and gives the corpus luteum a yellow tint. This color gradually fades, till at last all pigment is absorbed, and only the shreds of the basement or elastic membrane of the former follicle are left behind, imbedded in cicatricial fibrous connective tissue, the shrinkage of which causes a retraction at the surface of the ovary. The folded, homogeneous shreds are easily recognizable under the microscope by the deep carmine stain which they take up.

According to Bischoff, in most instances the formation of the follicles and the ova is completed in fœtal life or during the first few years after birth, and it is doubtful whether a new formation occurs in more advanced age. Out of the enormous number of follicles—Henle estimated in the ovary of a girl eighteen years old thirty-six thousand—probably many never reach full development. Beginning from early childhood, however, during the procreative period all stages of development of follicles and ova are found in the ovaries, the more fully developed lying in the deeper portions of the cortical substance. Upon reaching maturity the follicles occupy the whole width of the cortex, and even slightly protrude from the surface. The ovary after the menopause shows no follicles, but only dense, fibrous connective tissue, with a varying amount of the remains of follicular basement-membranes.

The connective tissue of the ovary is accumulated at its center, in connection with the hilus, through which the larger blood-vessels enter the stroma. The connective tissue is composed of interlacing bundles, plentifully supplied with smooth muscle-fibers. Only the peripheral portion of the ovary, the cortex, contains the follicular formations, and, at least in young individuals, the connective tissue of the cortex, between the follicles, is of the myxomatous variety. In older persons it has the character of fibrous tissue, which is most abundant at the periphery in the shape of a dense capsule. Such a tunica albuginea does not exist around the ovaries of children or of young animals (Waldeyer).

The *blood-vessels* of the ovary penetrate the hilus through the broad ligament; the largest amount of blood-vessels is found in

that part of the medullary portion which is nearest the cortex, and the latter receives capillaries almost exclusively. The arteries have a markedly spiral course and a broad muscle-coat, while the veins have very thin walls, and in the region around the hilus produce a rich plexus, approaching the cavernous structure. *Lymph-vessels* are also numerous, and, according to His, produce a closed reticulum, in the stroma as well as in the connective-tissue capsule of the follicles. Valves are found in the lymphatics outside the ovary, and also in the lymphatics of the broad ligament.

As *remains of embryonal formations* are considered:

(1) The *epoöphoron* (Rosenmüller), which lies in the lateral portion of the broad ligament, above the ovary, reaching to the hilus. It is composed of blind tubules, with a lining of columnar, ciliated epithelia. They are remnants of the sexual portion of Wolff's body.

(2) The *paroöphoron* (Waldeyer). This is located in the medial portion of the broad ligament, often extending to the lateral border of the uterus. It is likewise composed of tubules lined by columnar, ciliated epithelia, and is considered as the remains of the primordial kidney (Wolff's body).

(2) The *oviducts or Fallopian tubes* are composed of connective tissue, the innermost layer being the mucosa, the outermost the serosa, and between these are layers of smooth muscle-fibers. The mucosa has abrupt, longitudinal folds, which, toward the ampulla, are connected by oblique and transverse ridges, supplied with numerous smaller ledges. The portion nearest the epithelium is in young persons myxomatous, in older persons loose fibrous connective tissue, having longitudinal bundles of smooth muscles, more fully developed toward the uterine than toward the fimbriated extremity of the tubes. The submucous layer above the muscles is always fibrous connective tissue. The covering epithelia are ciliated columnar, extending over the fimbriæ, but, in human beings, not connected with the epithelia of the ovary. Of the muscle-layers the circular shows the most advanced development; the longitudinal, outside the circular, is composed of only a few scanty bundles. The subserous connective tissue is well developed, and bounded by the delicate but dense fibrous tissue of the peritoneum. The mucosa, close above the epithelium, has a rich reticulum of capillary blood-vessels.

(3) The *uterus* is composed mainly of smooth muscle-fibers, which toward the cavity are covered by the mucosa; at the periphery, in a great extent, by the peritoneum. The mucosa is

myxomatous connective tissue, crowded with lymph-corpuscles, so-called adenoid tissue, being uniform in structure throughout its breadth. The surface is smooth within the cavity, folded in the cervical canal, and supplied with conical papillæ on the external cervical portion; in the latter situation the mucosa is composed of delicate fibrous connective tissue, without lymph-corpuscles.

The mucosa of the uterus is lined with ciliated columnar epithelia, extending downward into the upper two-thirds of the cervical canal. Here, at somewhat varying depths, it blends with the stratified epithelium which covers the mucosa of the lower end of the canal and the external portion of the cortex. The larger plicæ palmatæ at their summits may exhibit stratified epithelium, while in the furrows between them columnar ciliated epithelia are present (Toldt). The surface epithelium sends numerous prolongations into the depth of the mucosa, producing the tubular *utricular glands,* which take a radiating and slightly winding course; many of these are bifurcated, and send off lateral branches. The lining epithelia of the glands are columnar ciliated, the current of the ciliary motion being spiral from the bottom toward the mouth of the gland (Lott). In the cervical canal the glands are less numerous than in the body of the uterus, and, besides the long, tubular formations, small pear-shaped glands are found, which are lined with short columnar or cuboidal epithelium. Their hypertrophy and occlusion is supposed to be the cause of the common cystic formations termed ovules of Naboth.

The muscle-layer of the uterus is composed of circular, longitudinal, and oblique bundles interlacing, without any apparent regularity. A regular arrangement into a middle circular layer, and internal and external longitudinal layers, can be traced in the cervical portion only. In the body of the uterus all layers contain circular and longitudinal bundles; these are more abundant, however, in the submucous and subserous layers, while in the middle portions of the uterine wall, especially at the place of transition of the cervical into the uterine cavity, the circular fibers are most numerous. An apparent boundary between the middle and the outer layers is established by the large number of arterial and venous blood-vessels, which are present in this situation. The subserous longitudinal fibers are partly continued into the broad ligaments, while the circular fibers can be traced into the initial portion of the round ligaments. The sub-

mucous muscle-bundles send delicate prolongations into the mucosa, and take a circular course around the openings of the Fallopian tubes.

The *arteries* of the uterus are marked by a winding, spiral course and a heavy muscle-coat; they branch usually at the boundary of the middle uterine muscle-layer — the so-called stratum vasculare. The capillary net-work is richest in the mucosa close above the epithelium. The veins are characterized by their thin walls and numerous sinuosities; they produce a narrow plexus in the stratum vasculare, and a coarse plexus on both sides of the body of the uterus. The lymphatics form a capillary plexus, with numerous blind terminations, in the mucosa, and another plexus in the subserous connective tissue, while the muscle-layers have fewer lymphatics. As to the termination of the nerves, nothing positive is known.

The tissue-changes that occur in menstruation are understood only in part, as shown by the following article. Still more obscure are the tissue-changes during pregnancy and involution. The source of the enormous new formation of myxomatous tissue, resulting in the production of the placenta and the very abundant increase of the muscle-tissue of the uterus in pregnancy, are still puzzles, notwithstanding the amount of literature treating of this subject.

The *pathology of the uterus* needs a more careful microscopical study than has yet been made. The origin of tumors to which it is subject is little understood. Among these are the common myo-fibroma, myxo-adenoma, myxo-angioma, as representatives of the benign type, and carcinoma — usually starting from the cervical portion, and exceptionally from the mucosa of the body and the fundus uteri — as a representative of the malignant type. Peculiar tumors are the lymph-adenoma or myxo-adenoma of the mucosa, which are considered to be the result of chronic endometritis. The tissue of these tumors — of which I have examined quite a number — consists of lymph-tissue with interspersed utricular glands; this structure bears a close resemblance to myxo-myeloma; and, nevertheless, experience teaches that by a thorough removal of the newly formed tissue with the curette a permanent cure can sometimes be obtained. The boundary between lymph-adenoma and myxo-myeloma has not yet been defined.

A peculiar complication, misleading the microscopist, occurred in the following case: Dr. D. brought me a tumor the size of a pigeon's egg, claiming that it was removed from the uterus. Under the microscope it proved to be *colloid cancer* — therefore, malignant. A few days later, Dr. M. brought shreds which he had gouged out from the "internal genitals"; microscopic examination revealed *cicatricial connective tissue* — therefore, something benign. Both specimens proved to have come from a lady with an ulcerating cavity behind the uterus, which had perforated the posterior cul-de-sac into the vagina. The main tumor was colloid cancer, evidently starting from the rectum, while the shreds had been removed from a place previously operated upon — therefore, a cicatrix. Dr. M., anxious to clear up the case, gouged out

other shreds from the cavity, and handed them to another microscopist, Dr. Dd., of this city, being known as a reliable man. He diagnosed *cicatricial tissue.* The tumor was then given him, and the diagnosis was *colloid cancer.*

MICROSCOPICAL STUDIES ON THE CATAMENIAL DECIDUA.

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At the present time, it is agreed by all histologists that no new formation of a tissue can take place except through embryonal elements. Morbid, as well as normal tissues, develop from an original indifferent or medullary formation, which is known to constitute the body of the animal embryo in the earliest stages of its existence.

Whenever one tissue is about to be transformed into another, the original one first breaks down into medullary elements — that is, it falls back into the earliest stage of embryonal development — from which a new tissue may arise.

The same process invariably takes place when, from an original normal tissue, a new formation starts. This new formation may be inflammatory in its nature, and, as such, limited in its course; or it may be a new formation without typical termination — a so-called neoplasm or tumor; it makes no difference, the process is the same.

The peculiar condition which sometimes occurs at the menstrual period, producing membranous discharges,— called "decidua catamenialis" or "dysmenorrhea membranacea,"— is known to be a new formation from the mucous membrane of either the uterus or vagina, or both. This process is independent of pregnancy. It is observed only at the time of menstruation, and is unquestionably caused by an irritation of the mucosa of the genital tract. This irritation is a constituent part of normal menstruation, and, as well-observed cases show, the only process which takes place whenever both ovaries are absent. This irritation must reach a higher degree than in normal menstruation, in order to produce a menstrual decidua.

My purpose is to present the anatomical features of uterine decidual membranes. The materials for my studies were found in the laboratory of Dr. Heitzmann, of this city; they consisted of five specimens. These had been preserved in alcohol, and, a few weeks before examination, had been placed in a weak solution of chromic acid — about one-sixth per cent. After sufficient hardening, the specimens were imbedded in a mixture of wax and paraffin, and were cut into thin sections for microscopical examination.

Under the microscope, all the specimens proved to be composed of medullary corpuscles and a relatively small amount of basis-substance, the latter in its myxomatous and fibrous varieties. The fibrous exhibited both the reticular arrangement and that of bundles composed of fine fusiform bodies in the earliest stage of development.

In all specimens, glandular formations of a tubular nature were present, lined by columnar ciliated epithelia — very probably the remains of original utricular glands, and not newly formed.

Under a power of five hundred diameters the medullary corpuscles presented mostly a globular shape; the globules were somewhat flattened at

* Abstract of the author's essay. *The American Journal of Obstetrics and Diseases of Women and Children*, vol. xv., April, 1882.

their parts of contact. Scattered among the globular elements were oblong, spindle-shaped formations, frequently arranged in clusters. All these bodies were invariably separated from each other, either by very narrow rims or by fields of a slightly granular substance, which fields were about the size of an original medullary corpuscle. Clusters of such medullary corpuscles were irregularly traversed and bounded by slender bundles of fibrous tissue. The medullary corpuscles did not appear uniform. Some were about the size of red blood-disks, and almost without structure; others were rather larger and indistinctly granular; others again, the largest, showed a distinct granulation and a central nucleus. The relative proportion of these three varieties varied greatly in the different specimens. In one case, the shining, homogeneous bodies were largely in excess. In another, the large, pale, granular bodies were most abundant, and the intervening spaces unusually broad. In a third case, the small, homogeneous bodies were scanty, while the pale, granular corpuscles were numerous, and about six times the size of the homogeneous ones. Their granulations were so coarse as to conceal the nucleus. The corpuscles exhibited a distinct arrangement in clusters, and between the clusters delicate fibrillæ could be traced, thus producing the appearance of myxomatous tissue. In a fourth specimen the smallest bodies were few in number; the large, granular ones surpassed in size the smaller by six or eight diameters. In many of these larger bodies the granulations were pale, evidently due to a formation of basis-substance, the nucleus very distinct, and the interstices had the appearance of a fibrous net-work resembling placental structure. The fifth case was so different from the others as to require a more detailed description.

High powers of the microscope (one thousand diameters) proved that this mass of embryonal corpuscles deserved the name of a tissue from the fact that all the bodies, of whatever size, were united by delicate filaments. No structure was defined in the smallest corpuscles. The larger ones showed vacuoles in their interior, while in the largest a reticulum could be traced whose points of intersection, with low powers, appeared to be granular. The reticulum was most marked in the finely granulated corpuscles with distinct nuclei, and the granulations within the nucleus also had the appearance of being connected in a net-like structure. The reticular formation crossing the plastids became continuous with all their neighbors through the delicate filaments traversing the light rims. The granular fields lying around these bodies exhibited only a faint reticulum; but still, this was united with the medullary corpuscles by the points arising from their peripheries.

Wherever fibrillæ were found, either in bundles or as a reticulum inclosing single or grouped corpuscles, these fibers were invariably composed of minute, spindle-like formations. These spindles showed a reticular structure, and were also joined to neighboring plastids by fine threads. (See Fig. 376.)

In the specimens of decidua studied by me, the smallest bodies represent the earliest stages of development of living matter, and from these globules arose the nucleated plastids, which were considerably enlarged from imbibition of a liquid. Here the living matter has passed into the reticular stage of development. In a more advanced condition the plastids had been transformed into basis-substance which was either fibrous or myxomatous in character, and remained traversed by a reticulum of living matter. The light fields around the medullary elements were made up of a myxomatous basis-

substance, and this substance composed the mass in which lay the unchanged central nuclei described in the fourth case.

Fibrous basis-substance may appear in the form of straight bundles inclosing myxomatous fields. It is obvious that in this condition the liquid contained in the original medullary corpuscles must have been transformed into a solid basis-substance, while the living matter itself remained unchanged. Living matter in a reticular arrangement first crosses the liquid, and afterward the interstitial solid basis-substance. The fibrous basis-substance is always composed of slender spindles, which indicate that the plastids had become elongated and divided up before a solidification of their liquid had taken place.

All specimens showed a varying amount of blood-vessels in longitudinal, transverse, and oblique sections. Capillary vessels were most abundant,

FIG. 376.—DECIDUA CATAMENIALIS.

M, nucleated medullary corpuscles; *S*, the medullary corpuscles split into spindles; *N*, such corpuscles transformed to basis-substance, the nuclei remaining unchanged; *E*, columnar ciliated epithelium of a utricular gland. Magnified 1000 diameters.

being recognized as such by their flat, endothelial lining. In one of the specimens scanty formations of vessels resembling arteries were observed. In another case, arterial vessels were unmistakably present, characterized by the muscular coat. All stages of arterial development could be traced. In some parts there were only cord-like formations with parallel outlines, composed of small medullary corpuscles which flattened each other, rendering their shape polyhedral. The outer corpuscles, seen in front view, appeared fusiform, so as to encircle the cord. Transverse sections of such a formation in some instances exhibited medullary bodies arranged in a radiating man-

ner, but without a clearly marked caliber. In other parts, a central light space could be discerned, evidently the first trace of the future lumen. This opening must have been produced by the vacuolation of the most inner medullary bodies. Some cord-like formations which, if viewed transversely, still appeared solid, when seen in longitudinal section, showed a narrow, central caliber, lined by delicate spindle-shaped bodies in lengthwise arrangement, corresponding to the endothelial coat of arteries. (See Fig. 377.)

In a more advanced stage of development, the artery had the appearance of a tube with a clearly marked caliber; but in the opening there could be seen clusters of granules or nuclei, evidently the remnants of former vacuoled medullary corpuscles.

In addition to these, other bodies were noticed within the caliber, discoid in shape, homogeneous and somewhat plicated, probably newly formed red

FIG. 377.—NEW FORMATION OF AN ARTERY IN DECIDUA CATAMENIALIS.

D, decidua elements, at their periphery transformed to basis-substance, the nucleus unchanged, *S*, spindle-shaped corpuscles, indicating the formation of an adventitial coat; *A*, shining, homogeneous elements in longitudinal section, the forming smooth muscles; the endothelia visible in the depth. Magnified 1000 diameters.

blood-corpuscles. In this stage of development, both the endothelial and muscular coat could be discerned in longitudinal and transverse sections of the vessels.

Of the existence of newly formed veins there could be no doubt, and some of them were filled with blood. These vessels were composed of an inner endothelial and an outer fibrous coat, the latter made up of fine fusiform bodies in longitudinal arrangement. Whether these formations could properly be considered smooth muscle-fibers, I am unable to decide.

The case furnished by Dr. Mundé was the fifth. He gave a history of a patient of his, a married lady, who menstruated only at intervals of three months, and who cast off decidual formations at every menstrual period. In microscopical examination of this case, it was seen that most of the medullary corpuscles were large and oval in shape. The fields of myxomatous basis-substance were abundant, and often holding in their midst coarsely granulated nuclei. The formation of a fibrous reticulum around the nucleated myxomatous fields and around the medullary corpuscles was more advanced than in any other case. In all sections obtained from these specimens I met with fields of tissue, consisting either of medullary elements or fibrous connective tissue, in which a peculiar change had taken place, into a shining, homogeneous mass, such as has been described as waxy degeneration. Capillaries and veins were also abundant, the latter being frequently engorged with blood, but no arteries could positively be distinguished. These features are not fully analogous to those of decidua reflexa or vera; and, from what I have observed, I should conclude, therefore, that the case was one of decidua catamenialis unusually far advanced in development, and almost approaching the features of decidua vera.

A positive discrimination between decidua menstrualis and decidua vera, in their earliest stages of formation, seems to be a matter of impossibility, as they have features in common. The development of fibrous connective tissue, as a rule, is farther advanced in decidua vera than in decidua catamenialis. Decidua vera, in its early stages — that is, up to the sixth or eighth week — is always characterized by the presence of a myxomatous structure uniformly distributed throughout the formation. Its circular or oblong spaces contain either large, finely granular plastids, with one or two nuclei, or a pale, indistinctly granular myxomatous basis-substance, in the center of which often an unchanged nucleus is visible. Not infrequently, in decidua vera, we meet with multinuclear bodies, whose significance is shown by Dr. J. W. Frankl. Finally, decidua vera is marked by the presence of villosities, which, running in all directions, are seen in longitudinal, transverse, and oblique sections.

Literature. According to H. Kundrat and G. J. Engelmann,* the hypertrophied mucosa of the uterus, during menstruation, overlaps the openings of the glands, with a marked increase of the size of the latter. The condition of rest of the uterus during the period of reproduction is of but short duration, as the mucosa commences to swell slowly before the menstruation, and slowly returns to rest after it. No new formation of blood-vessels could be observed in the mucosa of the uterus, swelled and hypertrophied in menstruation, but a considerable opacity and fatty degeneration of the cells takes place. The surface epithelium is preserved to the time of the fatty metamorphosis, but when this ensues, the epithelium of the mucosa, as well as that of the glands, is cast off to a considerable extent. In the first weeks of pregnancy, the mucosa — especially the inter-glandular tissue of the upper layers — develops to decidua, and the glands become elongated and enlarged.

G. Leopold † draws attention to the difference between membranaceous formations from the uterus and those from the vagina. The former are covered by columnar epithelia, and contain the characteristic glands, while the

* "Untersuchungen über die Uterus-Schleimhaut." Wiener Mediz. Jahrbücher, 1873.
† "Dysmenorrhœa Membranacea." Archiv f. Gynäkologie, 1876.

latter show only flat epithelia. He believes membranous dysmenorrhœa depends upon a diseased condition of the uterus, such as chronic metritis, fibrous tumors, or displacements. He says the tissue between the tubular glands consists of small, polyhedral or globular cells whose nuclei almost fill the bodies. Between these cells he found clusters of small, globular lymph-corpuscles. Evidently, he does not consider these cells to be decidual formations. He also found a few waving arteries in the midst of the membrane, and a great many capillaries close beneath the surface epithelia, where the hemorrhagic clots are situated. He agrees with Beigel in terming this condition chronic endometritis and endocolpitis exfoliativa.

J. Hoggan and F. E. Hoggan * draw attention to the difference between membranes cast off from the uterus and those from the vagina. In the former, utricular glands were present, and around them, in a transparent matrix or intercellular substance, embryonal cells in different stages of development were noticed. These writers also call attention to the presence of embryonal tissue below the epithelia of the normal uterus, which they consider to be morphologically identical with that of true decidua, as well as that of the dysmenorrhœic membrane.

Wyder † asserts that, in menstruation, the superficial layers of the mucosa are cast off, whereas the deep layers remain intact. A distinguishing feature between decidua vera and menstrualis is that, in the latter, the inter-glandular cells are small, round cells, almost completely filled by the nucleus, while in the former, the nucleus, in comparison with the protoplasm, remains small. He considers dysmenorrhœa membranacea (1) as a fibrous coagulum, (2) as a mucosa altered by endometritis, and (3) as a decidua of pregnancy.

The results of my studies of the structure of decidual formations are the following:

1. *Decidua menstrualis is formed by medullary or embryonal corpuscles, exhibiting a gradual development from a shining, globular, homogeneous mass of living matter into nucleated plastids.*

2. *Basis-substance, in decidua menstrualis, is always scanty. It may appear either in the myxomatous or fibrous varieties. In the former, it is slightly granular and apparently structureless; in the latter, it is either reticular or arranged in fibrous bundles. Both kinds of basis-substance are formations springing from the original medullary corpuscles.*

3. *Decidua catamenialis is traversed by a large number of blood-vessels, mostly capillaries. In some cases there is also a distinct new growth of arteries in such quantities as to greatly exceed the capillaries. Frequently, also, the formation of veins occurs.*

4. *Decidua catamenialis always contains glands of the tubular variety, lined by columnar ciliated epithelia. Very probably, these glands are not new formations, but simply the remains of the original utricular glands.*

5. *Decidua reflexa is composed of large medullary corpuscles, mostly of oval shape. The formation of a myxomatous and fibrous basis-substance is much further advanced, and the amount of venous blood-vessels much greater than in decidua catamenialis.*

6. *Decidua vera is made up of a freely vascularized and fully developed myxo-*

* "Pathology and Therapy of Dysmenorrhœa Membranacea." Archiv für Gynäkologie, 1876.

† "Beiträge zur normalen und patholog. Anatomie der menschl. Uterus-Schleimhaut. Archiv. f. Gynäkologie, Bd. xiii.

matous reticulum, in the meshes of which lie the nucleated decidual elements, or the myxomatous basis-substance holds the remnants of the decidual corpuscles. Fibrous connective tissue occurs mostly around the larger blood-vessels. Decidua vera is further characterized by the presence of villosities in different stages of development.

(4) *The Vagina and External Genitals.* The mucosa of the vagina is raised in folds (rugæ), and in this situation papillæ are present, while in the furrows between the folds the papillæ are small or absent. The papillæ are simple throughout the mucosa, but compound at the height of the rugæ and toward the vestibulum. The loose connective tissue in the deepest portions of the mucosa is dense, and somewhat looser in the outer layers. In the mucosa, varying numbers of lymph-corpuscles are found, arranged sometimes in circumscribed follicular formations. The covering epithelium is stratified, blending with that of the cervical portion of the uterus; no glands are present. The muscles are arranged in external and internal longitudinal and middle circular bundles, united by numerous fibers running in oblique directions; they are more developed in the posterior than in the anterior wall of the vagina. The outermost layers are composed of coarse bundles of connective tissue, with numerous elastic fibers. Blood- and lymph-vessels produce plexuses above the epithelial cover and below the muscle-layers, which themselves hold a large number of veins.

In the vestibulum the mucosa contains small, acinous, mucous glands, which are more numerous around the opening of the urethra and on the clitoris. The Bartholinian glands are also larger mucous glands. The hymen is a reduplication of the vaginal mucosa, sometimes very rich in blood-vessels and nerves. The labia minora are characterized by the presence of numerous sebaceous glands, which are absent in new-born children; their covering epithelium approaches the nature of the epidermis, since the innermost scales are destitute of nuclei. The transition of the mucosa into the external skin is completed on the labia majora, which are rich in smooth muscles and fat. The clitoris is covered by a mucosa, which, especially on the glans, is amply provided with tactile corpuscles and nerve-bulbs. The construction of its cavernous bodies is similar to those of the penis. C. Gussenbauer, after careful study, states that the nymphæ have a delicate, cavernous vascular system. The erectile tissue of the clitoris, according to him, is supplied with blood by small arteries at the root of the clitoris directly, and by arterioles and a

capillary net-work at the surface of the cavernous bodies, indirectly. The bulb of the vestibule is of the same structure as the cavernous bodies of the clitoris.

The *placenta and the umbilical cord* have been subjects of research in my laboratory, both as to their development and normal condition and their pathological changes. Some of the studies are not yet completed. The results of some investigations are laid down in the two following articles.

A Contribution to the History of the Development of the Human Decidua. By J. W. Frankl, M. D., New York.*

It is acknowledged that the placenta represents a connective-tissue formation belonging to the myxomatous variety. Formerly some histologists (Friedländer and others) were of the opinion that epithelial elements enter into the construction of the placenta; but since the publications of G. J. Engelmann and Hanns Kundrat, and recently of Gerhard Leopold, this view can no longer be maintained, and, with the exception of the epithelial covering of the villi of the placenta, we now scarcely look for epithelial bodies in the stroma, either in its villous or solid part.

The development of the placenta in its minutest elements has so far been very little studied. We know, since the publication of W. Reitz†, that the villi are originally solid masses, without any differentiation into stroma, blood-vessels, and covering epithelium, which differentiation they present only with the advancing growth of the embryo. Indeed, it is easy to satisfy one's self about the correctness of the assertions of Reitz on growing placentæ of the second, third, and fourth months, where formed villosities are already to be seen, beset with more or less distinctly pediculated buds of a uniform structure. But how the solid part of the placenta, that nearest to the amnion, advances in growth, especially the formation of the myxomatous basis-substance, has not yet been elucidated.

Engelmann and Kundrat ‡ described the peculiar clusters of large decidua-cells occurring in the growing decidua-layer of the placenta. They consider these clusters as being in connection with the development of the villi.

Gerhard Leopold § repeatedly mentions their presence, and suggests that these clusters, as he asserts, most numerous in the fifth month of development of the placenta, are split into smaller and larger cells. How this is done he does not say.

George Hoggan and Frances Elizabeth Hoggan ‖ also conclude that the large, so-called embryonic multinuclear "decidua-cells" give rise to the formative cells of the decidua, but they do not specify their view, nor describe the way in which the latter originate from the former.

* Abstract of the author's paper. *American Journal of Obstetrics and Diseases of Women and Children*, vol. xi., October, 1878.

† "Sitzungsberichte der Kais. Akad. d. Wissenschaften in Wien," Bd. lvii.

‡ "Untersuchungen über d. Uterus-Schleimhaut." Wiener mediz. Jahrbücher, 1873.

§ "Die Uterus-Schleimhaut während der Schwangerschaft und der Bau der Placenta." Arch. f. Gynäkologie, ii. Th., Bd. xi.

‖ "Zur Pathologie u. Therapie d. Dysmenorrhœa membranacea." Arch. f. Gynäkologie, Bd. x.

In the growing placenta we always meet in the decidua-layer with multinuclear masses, sharply marked from the surrounding myxomatous basis-substance. These clusters are numerous in earlier stages of the developing placenta, where the decidua itself is only of a relatively small diameter; while the fully developed placenta, in its solid part, is of a noticeable width, but altogether devoid of the clusters above mentioned. On the contrary, single elements, surrounded by the net-work of the myxomatous connective tissue, are present only in a comparatively small number in the growing decidua, while they constitute the whole solid part of the fully developed placenta. This fact led the authors to the conclusion that the isolated decidua-elements originate from multinuclear clusters.

The only way to examine a placenta, in my opinion, is to cut the tissue with a razor after it has been sufficiently hardened by a repeatedly changed one-half per cent. chromic acid solution. I cannot advocate the picking method of the villous portion, and still less, of course, that of the decidua. By cutting we oftentimes succeed in obtaining thin sections of the villosities in different directions, perfectly fit for examination even by the highest powers of the microscope. Such sections are easily made through the solid part of the placenta; while picking will always bring to view *débris* of the tissue only, as a rule mangled to such an extent that a close examination under the microscope is a matter of impossibility.

Specimens obtained from the solid part of a placenta of the six months' development, with a power of about 500 diameters, show a great number of bioplasson formations, partly built up by large nucleated elements, partly by a uniform granular mass, in which there are imbedded nuclei in a more or less varying number. Besides, we meet with clusters, in which nuclei cannot be recognized, but a differentiation into smaller granular spindle-shaped elements can be traced out. These masses, as a rule, are distinctly bounded toward the surrounding myxomatous basis-substance, which, owing to its apparently homogeneous, highly refracting structure, is a well-defined formation. The net-work of the myxomatous connective tissue is partly loose and delicate, including in almost every mesh a granular plastid, this being either provided with or devoid of a nucleus, while in other places the myxomatous net-work is very heavy, its meshes being narrow and filled with a light, apparently homogeneous, structureless-looking substance. A still higher development of the connective tissue can be found only around the arteries, the adventitia of which is a combination of myxomatous with fibrous connective tissue, inasmuch as bundles of delicate fibers form an elongated net-work, and in the meshes of these again granular, partly nucleated plastids are visible. The veins, on the contrary, being sinuous and irregular in their outlines in a hardened specimen, are directly surrounded by loose myxomatous connective tissue.

Sections made through the solid part of a placenta of nine months, if seen with a power of 500 diameters, show the complete absence of clusters, the "giant-cells" of the authors, and the whole tissue is decidedly myxomatous in structure. The meshes of this tissue are partly filled with single, chiefly nucleated plastids, many of which, owing to the prevalent amount of basis-substance, are very narrow, and contain a light, apparently structureless substance. Besides, a considerable amount of fibrous tissue is to be seen principally in the neighborhood of arteries, the adventitia of which is altogether fibrous in structure. Where several arteries run through the stroma

near each other, the adventitial layer, common to all, consists mainly of fibrous structure, between which relatively small bridges of myxomatous tissue are left.

Let us now examine the formations in the solid part of the placenta with the magnifying power of 1200 diameters, beginning with a six-months' placenta. (See Fig. 378.)

The stroma is built up by bioplasson, arranged in the shape of multinuclear bodies, and by the basis-substance. The latter, looking homogeneous or finely granular with a low power, proves to be formed by extremely small spindles closely packed together, if seen with a high power. These spindles are united with each other by delicate threads running vertically through all the trabeculæ of the basis-substance. In the meshes of the reticular basis-substance, again, we find round or oblong plastids.

FIG. 378.—HUMAN PLACENTA OF SIX MONTHS.

M, multinuclear bioplasson cluster, *C*, delicate fibrous connective tissue; *D*, plastids in transition to a myxomatous basis-substance. Magnified 1200 diameters.

Wherever we meet with bioplasson, its structure, as first described by C. Heitzmann, is plainly visible. Coarse granules present in the middle of nuclei, the so-called nucleoli, send out radiated spokes, through which they are united with the neighboring smaller granules. Again, these granules are united with each other and with the shell of the nucleus by means of delicate threads. The shell of the nucleus, being either a smooth or granular layer, although continuous under all circumstances, projects very minute radiated offshoots, which traverse the light seam around the nucleus, and run to the next granules of the bioplasson body. All granules of the latter are united more or less distinctly by fine threads, so much so that a delicate net-work is established throughout the corpuscles. Where bioplasson meets with

basis-substance, we always see numerous fine threads projecting into the basis-substance, where they are lost to sight.

In the fully developed decidua the details in the structure are exactly the same as in the growing placenta, with one exception — viz.: that multinuclear masses are absent; the meshes of the myxomatous basis-substance containing roundish plastids, mainly devoid of nuclei, while numerous meshes, surrounded by a dense, highly refracting net-work of the basis-substance, look homogeneous and structureless. The basis-substance assumes, in the adventitial layer of the arteries, a decidedly fibrous structure, which again proves to be constructed by bundles of minute spindles, in the narrow and elongated meshes of which granular bioplasson is to be seen. The interstices between these spindles of the fibrous basis-substance are also traversed by minute vertical threads.

The history of the development of the basis-substance has always been a matter of careful study with our best histologists. Now, the placenta offers an excellent means of settling several points of discussion, both on account of the relatively short time required for its formation, and the clearness of the relation between the protoplasm and the myxomatous basis-substance.

The manner of formation of the myxomatous basis-substance of the placenta is as follows:

The formative elements appear in the shape of multinulear bodies, exactly like those in developing bone or cartilage where the so-called "giant-cells" prove to be the forerunners of the forming basis-substance. The next step is the formation of bioplasson layers, in which nuclei are no more recognizable, while the net-work of living matter is arranged mainly in a longitudinal direction — viz.: in the shape of closely packed spindles. In the next stage the fluid part of the plastids is transformed, chemically, into a shining, highly refracting basis-substance which hides the living matter, this being demonstrable only in the interstices between the delicate spindles in the shape of minute grayish threads.

The most solid part of the basis-substance, as represented by the fibrous tissue of the adventitia of the arteries, originates in the same way as the myxomatous basis-substance of the stroma of the decidua. The only difference is that the groups, respectively the net-work of the living matter, are more elongated in the adventitial fibrous than in the myxomatous reticular tissue. In both instances the meshes hold a certain amount of unchanged bioplasson, which is relatively profuse in the myxomatous tissue and scant in the fibrous. Even in the latter tissue we find larger and more numerous bioplasson masses in the decidua of the placenta, advanced only to the fifth or sixth month of development, than in the decidua fully ripe for elimination from the maternal body.

Waxy Degeneration of the Placenta. By Jeannette B. Greene, M. D., New-York.*

My attention was drawn by Dr. Heitzmann to the fact that specimens of placenta from cases of premature birth and abortion, which had been presented to him by different physicians, exhibited peculiar changes in their

* Abstract of the author's essay. *American Journal of Obstetrics and Diseases of Women and Children*, vol. xiii., 1880.

structure. Although to the naked eye these appearances resemble those of fatty degeneration, the microscope showed the morbid condition to be that of waxy rather than fatty degeneration.

The subject appeared to be of sufficient interest to bestow a few weeks upon its investigation. I had at my disposal ten placentæ of the following ages:

First. A placenta of six or seven weeks, fœtus attached. This placenta was a solid, clumsy-looking mass. Its substance had in some places been entirely transformed into a grayish-yellow material, of a shining appearance; in other parts the shining material appeared only in scattered foci.

Second. A three-months' placenta, which had been detached from the uterine wall six weeks after abortion, a severe hæmorrhage having occurred. In this placenta there was no perceptible change to the naked eye. To the touch the mass appeared rather denser than normal placental tissue.

Third. A four-months' placenta. A portion of this placenta, with the umbilical cord attached, came under my observation. This specimen exhibited the same general characteristics as the others — the same yellowish patches scattered throughout the placenta. The decidual portion had been extensively invaded by a yellowish material, varying greatly in width in different parts. The amniotic surface had a mottled appearance and was deeply corrugated.

Fourth. A five-months' placenta, together with the fœtus. This specimen. normal in its main mass, showed in the decidual portion small, homogeneous patches of a yellow color, and in the villous portion scattered points, also of a yellowish color.

Fifth. A flesh mole, fifth month of pregnancy. This specimen was a mass about the size of the fœtal head at term. It was irregularly lobed, and consisted principally of hæmorrhagic clots. Within the tissues on the periphery, and between the clots, remains of the decidua were to be seen, of a grayish-yellow color. The fœtus was lost.

Sixth. A six months' placenta. Several microscopical specimens were sent to the laboratory for examination. These specimens exhibited the same general characteristics observed in the other cases.

Seventh. A placenta of seven months. The whole placenta was paler than normal, and the entire tissue, both decidual and villous, presented a decidedly glistening and lardaceous appearance. There were no isolated spots of degeneration. The attached cord was somewhat œdematous. The cross-section presented the same lardaceous appearance observed in the placenta.

Eighth. A seven-months' placenta. This placenta was coarsely lobulated, and of a consistency and thickness greater than normal. The entire tissue, but chiefly the decidual portion, was of a yellow color, greatly resembling fat in appearance. The umbilical cord presented no changes of any kind. Fœtus died soon after delivery.

Ninth. A placenta of eight months. There was no change in the villous portion, and in the decidual portion only an occasional spot of yellowish discoloration. Fœtus lived.

Tenth. An eight-months' placenta. The decidual portion presented a lardaceous appearance; the remaining tissues were normal. Fœtus living at birth.

In all cases in which the yellow discoloration was apparent, the diagnosis made without the aid of the microscope was fatty degeneration of the pla-

centa. For many years this condition was thought to have been the principal cause of abortion or premature birth, resulting in the death of the fœtus, either within the uterus or soon after delivery.

Although the fœtus might have the appearance of being well developed, its death, as a rule, occurred whenever the degeneration in the placenta was observable. In many instances the miscarriage was habitual, taking place at about the same period of pregnancy; the fœtus never being perfectly developed.

The ten placentæ above described were furnished either in a fresh condition or preserved in alcohol. All these placentæ were placed in a half per cent. watery solution of chromic acid for hardening.

Specimens obtained from placentæ which had undergone a high degree of degeneration — Cases one, three, and eight — exhibited with the lower power of the microscope the following appearances: the decidual tissue contained sharply defined patches of a grayish or yellow color with a peculiar luster. These patches were of a uniform structure, with only a slight trace of decidual tissue remaining, and they were built up by irregular, jagged globules closely crowded together, strongly resembling fat in color and in general appearance. Toward the decidua these morbid spots were in some places distinctly defined, in other places were bounded by tissues, in which the morbid change was of a less marked degree.

In the villosities the degenerative change is rarely found, but, if found, it is, as a rule, only in the parts in immediate connection with the decidua. In those rare instances where the degeneration did occur, it was not found to pass beyond the reticular or homogeneous stage — that is, it did not lead to the transformation of the myxomatous tissue into globular clusters.

The decidual portion of the three placentæ, which exhibited the highest degree of the homogeneous degeneration, showed also a greater development of fibrous connective tissue than is to be found in the normal placenta of the same age.

Within the fibrous, and also within the myxomatous basis-substance, but in a lower degree, the oblong decidual elements showed a coarse granulation, so as to entirely conceal the central nucleus. The granules resembled fat in their high degree of refractive power. In the villosities, those which had an unchanged myxomatous structure showed the normal amount of blood-vessels and capillaries; while in those villosities, in which the homogeneous degeneration was marked, scarcely any trace of blood-vessels was to be found.

Higher powers of the microscope, five hundred to six hundred, showed a homogeneous change of the basis-substance, with coarsely granular plastids, almost unchanged. A slight formation of connective tissue was observable encircling the villosities, and irregularly scattered between and within them; in the latter position, however, barely traceable. This tissue showed small plastids with nuclei, also apertures, indicating the caliber of former capillaries. The greater part of these vessels, had, however, entirely disappeared.

A power of twelve hundred immersion plainly revealed the nature of the morbid change. The basis-substance was divided into irregular fields of shining appearance; between these fields the bioplasson was unaltered, exhibiting its characteristic, net-like structure. (See Fig. 379.)

This reticulum was also traceable within the fields; here, however, the meshes were larger than those in the unchanged portions. This net-like

structure disappears altogether only in the highest degree of the degeneration, where nothing is to be seen but shining, structureless masses, with high refracting power. The bases of the villosities are either of the same structure as the decidua, or they show a slightly fibrous basis-substance interspersed with plastids. No blood-vessels can be traced in this part. In some villosities irregular openings are observable, evidently the remains of capillary blood-vessels, which, in the degenerative condition, serve only for the passage of plasma, and not for the circulation of the blood-corpuscles.

The question arose: What was the nature of this degeneration?

In order to settle this inquiry, a number of reagents were employed. An *ammoniacal solution of carmine* changed the homogeneous masses in the basis-substance only in specimens where the degeneration had not reached a high

F

FIG. 379.—WAXY DEGENERATION OF THE PLACENTA.

T, decidual tissue in a high degree of waxy metamorphosis, *V*, basis of a villus with clefts, probably the remains of vessels, *F*, basis of a villus with fibrous basis-substance, *B*, basis of a villus in a high degree of waxy metamorphosis. Magnified 1200 diameters.

degree, and which had not been kept any length of time in chromic acid solution; in the latter the homogeneous masses took on a yellow, almost a green color, and were unaffected by the carmine. Carmine is, therefore, an excellent reagent for bringing into view the homogeneous fields, as the carmine readily stains the normal portions of the tissue. The shining granules in the decidual elements also remain unchanged. The carmine-stained specimens were left in absolute alcohol for a short time — twenty-four hours; they were then dipped in oil of cloves, returned to the alcohol for a short time, and finally placed in water for mounting in glycerine. In these speci-

mens, the homogeneous fields and clusters, even in the highest degree of the degeneration, remained perfectly unchanged. Those decidual elements which had before shown coarse, shining granules, after treatment with oil of cloves, lost in a great measure their granular appearance; clearing up to such an extent that the reticular structure of the bioplasson became again visible with the highest powers of the microscope. A few of the granules in these specimens, however, showed a lower refracting power than fat. Such granules were also found in the connective tissue, joined to the neighboring net of living matter by means of fine threads. Specimens stained with carmine, taken from the alcohol and placed in spirit of turpentine, showed the same results as after treatment with oil of cloves.

After having thoroughly washed the specimens in distilled water to remove the chromic acid stain, a half per cent. solution of *chloride of gold* was applied for one hour, and they were then removed. After a few days the normal basis-substance exhibited a slight purple color. The homogeneous fields and clusters took on a dark-blue tint, which became deeper after exposure to the sunlight. The coarse granules in the decidual elements did not change their color.

On application of *tincture iodine*, the homogeneous fields became tinged with a brown color. The addition of sulphuric acid produced no effect upon this coloration.

Fuchsine, in a concentrated solution, gave a darker hue to the homogeneous fields than it did to the normal basis-substance. Dark crimson globules were scattered through the decidual elements, which gave a beautifully spotted appearance to the specimen.

Violet methyl aniline, in strong solution, stained the normal tissue a dark blue color, at the same time giving to the homogeneous fields a reddish hue, which varied in intensity according to the degree of morbid change—being darker where the degeneration was most strongly marked. This red color was most noticeable with low powers of the microscope.

Osmic acid, in a one per cent. solution, stained the whole specimen brown. The homogeneous fields and strings, in many places, did not differ in their color from the adjacent tissues, while in other parts they had assumed a darker hue. The shining granules scattered in the decidual elements, through this re-agent became very dark brown—almost black.

Picrate of indigo gave to the specimens a uniform light green color; the homogeneous fields and strings were stained a deep grass-green.

From the above observations and experiments it follows that, in all the placentæ here described, a peculiar change had taken place in the basis-substance of the placental tissue, which change bears a close resemblance, in all essential characteristics, to waxy degeneration as it occurs in other organs. In a few placentæ only was there a fatty change in the decidual elements, and this change certainly was of much less extent than the waxy degeneration.

Waxy degeneration is obviously a morbid chemical change of the myxomatous basis-substance. The nature of this change is almost unknown, although its analysis has been attempted by very good chemists. The assertion that it is de-alkalized fibrine is merely hypothesis. The net-work of living matter is preserved to a certain extent, except in cases where the waxy degeneration is in its most advanced stage. In these cases the reticulum of living matter appears completely lost.

While the waxy degeneration is located in the basis-substance only, the fatty degeneration, on the contrary, is found almost exclusively in the living matter. With high powers of the microscope we plainly see the granules of living matter within the decidual elements first increase in size, and gradually taking the peculiar shining appearance so characteristic of fat. At first the shining fat-granules remain in unbroken connection with the neighboring reticulum of living matter; afterward the granules appear to be freed from their union with the reticulum, and finally they coalesce and produce oil-globules. Even in the highest degree of degeneration the living matter never seems to be entirely lost. This is demonstrated by the treatment of the specimens with oil of cloves or turpentine, all fat being destroyed by these re-agents.

In nearly all decidual elements a scanty reticulum of living matter may be traced, and in some parts with enlargements at the points of intersection; and in these enlargements coarse granules are frequently seen.

The re-agents indicate that there must be a slight difference between the waxy mass of the placenta and the waxy degeneration we find in the kidneys, liver, and spleen. It appears that, in the above-mentioned organs, the chemical change which takes place in the basis-substance differs somewhat from that which takes place in the placenta; the difference, however, is too insignificant to alter either the change itself or its results in the placental tissue.

In placenta No. 7, the *amnion* in those parts in immediate contact with the decidua of the placenta, was affected with morbid changes identical with those observed in the placenta itself. Scattered through the amnion were shining, homogeneous bodies, also rod-like formations, which were in continuity with the connective tissue of the amnion. The homogeneous bodies were either round or oblong, showing a central nucleus, but by no means so distinctly stratified as are the amylaceous corpuscles of the arachnoid. It may be that these forms are the remains of bioplasson bodies whose fluid has been transformed into a waxy mass.

In the *umbilical cord* of this placenta I observed a peculiar change starting in the portion attached to the placenta and extending two or three inches. In the periphery of the cord the myxomatous tissue was fully developed, while the tissue in the vicinity of the umbilical arteries showed considerable enlargement of its meshes — the so-called dropsy of the cord. The meshes were surrounded by extremely fine fibers, and crossed by a peculiar, shining, yellow reticulum, inclosing empty spaces. In connection with the bundles of fibers that surrounded the meshes, coarser or finer trabeculæ were observed, which showed shining enlargements at the points where the trabeculæ were cut transversely. In some regions delicate, pediculated buds and club-like projections, or rosary-like chains, were seen. These formations took up the stain of fuchsine very readily, and were unaltered by treatment with turpentine and alcohol. (See Fig. 380.)

It seems obvious, therefore, that this change of the umbilical cord which I have studied is due to waxy degeneration of the reticulum of the myxomatous tissue, together with liquefaction of the basis-substance.

The *literature* of the subject of my researches is extremely meagre.

Carl Rokitansky * mentions amyloid degeneration of the placenta, without further details. He is the only observer who speaks of such a degeneration.

* "Manual of Morbid Anatomy," chapter on "Anomalies of the Placenta." Vienna, 1861.

Carl Wedl,* on page 170, says: "The most striking morphological changes are those which occur in connection with miscarriages from the sixth to the ninth month, when the fœtus is dead. The most usual alteration consists in an accumulation of a dark-yellowish or grayish-brown molecular substance, which renders the villi, with their clavate extremities, almost opaque, or merely diminishes their proper transparency at this point. This metamorphosis of the villi usually extends over entire groups, and it may be very strongly marked in many parts of the placenta, while in others it is very faintly indicated or entirely absent. It is more developed on the convex than on the concave sides of the placenta, and is associated with an absence of blood in the affected portions." On page 171, he says: "The degree to which the atrophy has advanced may be estimated by the extent to which this kind of

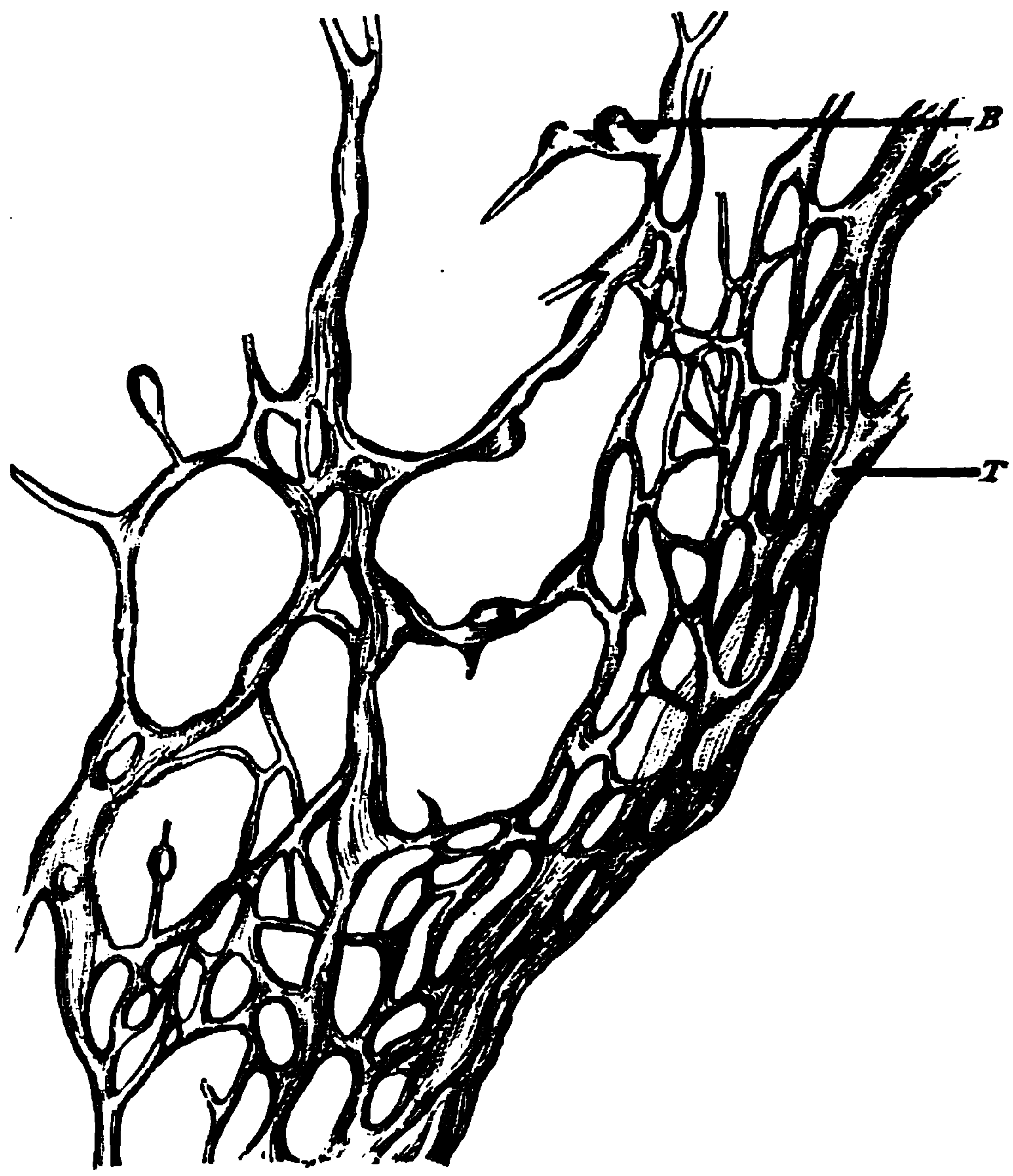

FIG. 380.—WAXY DEGENERATION OF THE UMBILICAL CORD.

T, trabeculæ of the myxomatous tissue; *B*, knob-like projections. Magnified 1200 diameters.

metamorphosis can be traced toward the thicker stem of the villi. The connective-tissue elements of the stem are frequently in a state of fatty degeneration — that is to say, brilliant molecules of considerable size are visible in the fiber-cells, from which the nucleus has escaped — or a chain of fatty molecules may be seen in the more slender fusiform fibers."

Carl Hennig † speaks of fatty degeneration of the decidua vera in the

* "Rudiments of Pathological Histology." London, 1853.

† "Studien über den Bau der menschl. Placenta und über ihr Erkranken." Leipzig, 1862; *Schmidt's Jahrb.*, 1873.

last months of pregnancy. Morbid, fatty degeneration occurs, according to this writer, in the vera serotina placentæ, often also in the villi; in persons of impaired health, this degeneration accompanies inflammation of the placenta, the vesicular mole, and syphilis; the result being abortion or premature birth. No allusion is made to amyloid degeneration.

The conclusions drawn from the examination of the ten placentæ are:

First. That the change in the placenta so productive of abortion and premature birth is a waxy, and not a fatty degeneration, as heretofore believed.

Second. Among the ten placentæ in waxy degeneration, three only, in the highest degree of this morbid change, exhibited signs of fatty degeneration also, and this latter condition was always much less marked than the former.

Third. The waxy degeneration consists in a peculiar chemical alteration in the myxomatous basis-substance, both in the solid and the villous portions of the placenta.

Fourth. The degeneration is kindred to that which occurs in the liver, spleen, and kidneys of so-called dyscratic or cachectic individuals. The plastids of the decidua and the villosities also enter the waxy degeneration in their fluid portion. The net-work of living matter is not affected by this change, except in its higher degrees, where the living matter completely disappears.

Fifth. Fatty degeneration results from a chemical change of the living matter at the points of intersection of the net-work—the so-called granules. At first the fat-granules are joined to the neighboring reticulum by means of fine threads; afterward, the fat-granules coalesce and produce fat-globules.

Sixth. Waxy degeneration of the placenta is sometimes combined with an analogous degeneration of the amnion and the umbilical cord. In the cord it appears in the form of a shining reticulum arising from the degeneration of the fibrous net-work of the myxomatous basis-substance.